# THE AMERICAN JOURNAL OF PSYCHIATRY

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By Joseph C. Wu and William E. Bunney

Differential Diagnosis and Classification of Apathy

By Robert S. Marin

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**Brief Summary of Prescribing Information.**

**Indications and Usage:** Management of anxiety disorders or short-term relief of symptoms of anxiety or anxiety associated with depressive symptoms. Anxiety or tension associated with stress of everyday life usually does not require treatment with an anxiolytic.

Effectiveness in long-term use, i.e., more than 4 months, has not been assessed by systematic clinical studies. Reassess periodically usefulness of the drug for the individual patient.

**Contraindications:** Known sensitivity to benzodiazepines or acute narrow-angle glaucoma.

**Warnings:** Not recommended in primary depressive disorders or psychoses. As with all CNS-acting drugs, warn patients not to operate machinery or motor vehicles, and of diminished tolerance for alcohol and other CNS depressants.

Physical and Psychological Dependence: Withdrawal symptoms like those noted with barbiturates and alcohol have occurred following abrupt discontinuance of benzodiazepines (including convulsions, tremor, abdominal and muscle cramps, vomiting and sweating). Addiction-prone individuals, e.g. drug addicts and alcoholics, should be under careful surveillance when on benzodiazepines because of their predisposition to habituation and dependence. Withdrawal symptoms have also been reported following abrupt discontinuance of benzodiazepines taken continuously at therapeutic levels for several months.

**Precautions:** In depression accompanying anxiety, consider possibility for suicide.

For elderly or debilitated patients, initial daily dosage should not exceed 2mg to avoid oversedation. Terminate dosage gradually since abrupt withdrawal of any antianxiety agent may result in symptoms like those being treated: anxiety, agitation, irritability, tension, insomnia and occasional convulsions. Observe usual precautions with impaired renal or hepatic function. Where gastrointestinal or cardiovascular disorders coexist with anxiety, note that lorazepam has not been shown of significant benefit in treating gastrointestinal or cardiovascular component. Esophageal dilation occurred in rats treated with lorazepam for more than 1 year at 6mg/kg/day. No effect dose was 1.25mg/kg/day (about 6 times maximum human therapeutic dose of 10mg/day). Effect was reversible only when treatment was withdrawn within 2 months of first observation. Clinical significance is unknown; but use of lorazepam for prolonged periods and in geriatrics requires caution and frequent monitoring for symptoms of upper G.I. disease. Safety and effectiveness in children under 12 years have not been established.

ESSENTIAL LABORATORY TESTS: Some patients have developed leukopenia; some have had elevations of LDH. As with other benzodiazepines, periodic blood counts and liver function tests are recommended during long-term therapy.

CLINICALLY SIGNIFICANT DRUG INTERACTIONS: Benzodiazepines produce CNS depressant effects when administered with such medications as barbiturates or alcohol.

CARCINOGENESIS AND MUTAGENESIS: No evidence of carcinogenic potential emerged in rats during an 18-month study. No studies regarding mutagenesis have been performed.

PREGNANCY: Reproductive studies were performed in mice, rats, and 2 strains of rabbits. Occasional anomalies (reduction of tarsals, tibia, metatarsals, malrotated limbs, gastroschisis, malformed skull and microphthalmia) were seen in drug-treated rabbits without relationship to dosage. Although all these anomalies were not present in the concurrent control group, they have been reported to occur randomly in historical controls. At 40mg/kg and higher, there was evidence of fetal resorption and increased fetal loss in rabbits which was not seen at lower doses. Clinical significance of these findings is not known. However, increased risk of congenital malformations associated with use of minor tranquilizers (chlordiazepoxide, diazepam and meprobamate) during first trimester of pregnancy has been suggested in several studies. Because use of these drugs is rarely a matter of urgency, use of lorazepam during this period should almost always be avoided. Possibility that a woman of child-bearing potential may be pregnant at institution of therapy should be considered. Advise patients if they become pregnant to communicate with their physician about desirability of discontinuing the drug. In humans, blood levels from umbilical cord blood indicate placental transfer of lorazepam and its glucuronide.

NURSING MOTHERS: It is not known if oral lorazepam is excreted in human milk like other benzodiazepines. As a general rule, nursing should not be undertaken while on a drug since many drugs are excreted in milk.

**Adverse Reactions,** if they occur, are usually observed at beginning of therapy and generally disappear on continued medication or on decreasing dose. In a sample of about 3,500 anxious patients, most frequent adverse reaction is sedation (15.9%), followed by dizziness (6.9%), weakness (4.2%) and unsteadiness (3.4%). Less frequent are disorientation, depression, nausea, change in appetite, headache, sleep disturbance, agitation, dermatological symptoms, eye function disturbance, various gastrointestinal symptoms and autonomic manifestations. Incidence of sedation and unsteadiness increased with age. Small decreases in blood pressure have been noted but are not clinically significant, probably being related to relief of anxiety.

Transient amnesia or memory impairment has been reported in association with the use of benzodiazepines.

**Overdosage:** In management of overdosage with any drug, bear in mind multiple agents may have been taken. Manifestations of overdosage include somnolence, confusion and coma. Induce vomiting and/or undertake gastric lavage followed by general supportive care, monitoring vital signs and close observation. Hypotension, though unlikely, usually may be controlled with Levarterenol Bitartrate Injection U.S.P. Usefulness of dialysis has not been determined.

**DOSAGE: Individualize for maximum beneficial effects. Increase dose gradually when needed, giving higher evening dose before increasing daytime doses. Anxiety, usually 2-3mg/day given b.i.d. or t.i.d.; dosage may vary from 1 to 10mg/day in divided doses. For elderly or debilitated, initially 1-2mg/day; insomnia due to anxiety or transient situational stress, 2-4mg h.s.**

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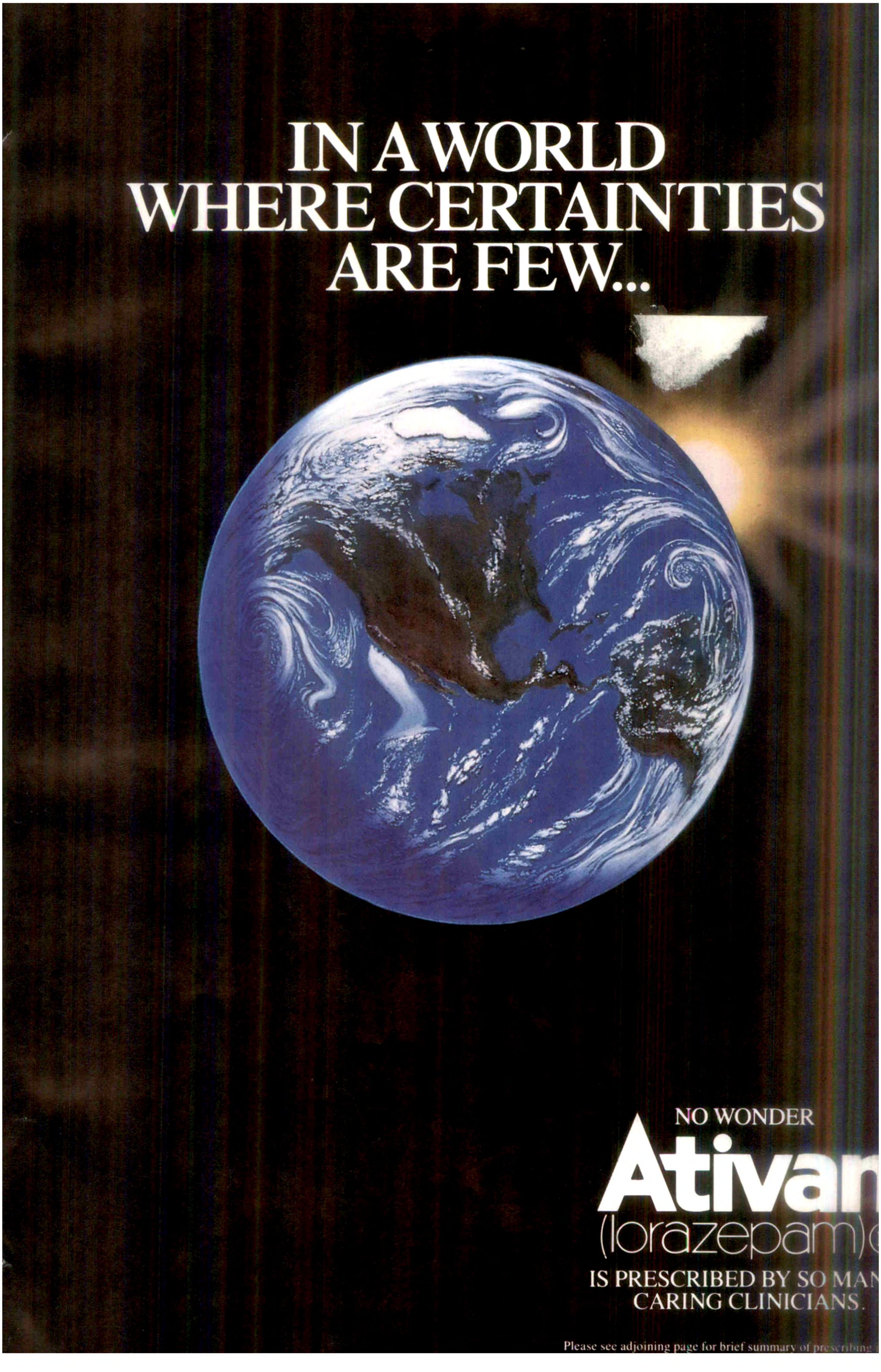
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8:00 a.m.-9:45 a.m.
***The Neurobiology of Depression***

9:45 a.m.-11:30 a.m.
***The Genetics of Depression***

11:30 a.m.-Noon
***Complimentary Luncheon***

Noon-2:00 p.m.
***Treating Depressive Disorders***

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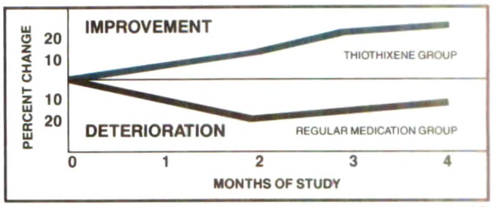

(Adapted from DiMascio and Demirgian[2,3])

Forty-two psychotic male and female patients under age 55 were entered in this study on a nonblind basis, and randomly assigned to their regular medication or switched to thiothixene. Patients were evaluated at baseline and on a daily basis, and periodically rated on the Global Improvement and Brief Psychiatric Rating Scales.

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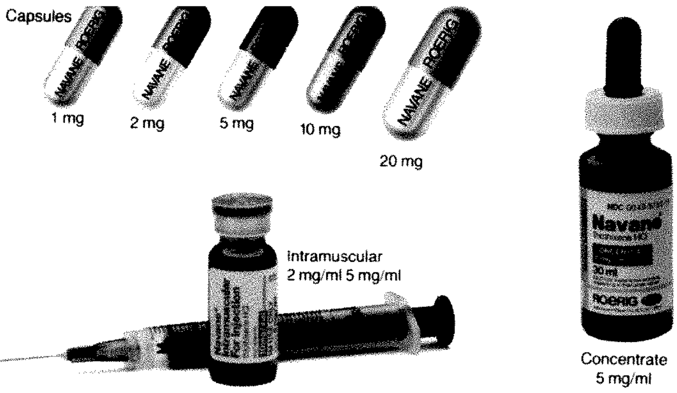

**References:** 1. Bressler B, Friedel RO: A comparison between chlorpromazine and thiothixene in a Veterans Administration hospital population. *Psychosomatics* 1971;12:275-277. 2. DiMascio A, Demirgian E: Study of the activating properties of thiothixene. *Psychosomatics* 1972;13:105-108. 3. DiMascio A, Demirgian E: Job training in the rehabilitation of the chronic schizophrenic. Presented as a Scientific Exhibit at The American Psychiatric Association, Washington, DC, May 3-6, 1971. 4. Goldstein B, Weiner D, Banas F: Clinical evaluation of thiothixene in chronic ambulatory schizophrenic patients, in Lehmann HE, Ban TA (eds): *The Thioxanthenes: Modern Problems of Pharmacopsychiatry.* Basel, Switzerland, S. Karger, 1969, vol 2, pp 45-52. 5. Dillenkoffer RL, Gallant DM, George RB, et al: Electrocardiographic evaluation of schizophrenic patients: A double-blind comparison. Presented as a Scientific Exhibit at The 125th Annual Meeting of the American Psychiatric Association, Dallas, May 1-4, 1972. 6. Data available on request from Roerig.

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**Indications:** Navane is effective in the management of manifestations of psychotic disorders. Navane has not been evaluated in the management of behavioral complications in patients with mental retardation.

**Contraindications:** Contraindicated in patients with circulatory collapse, comatose states, central nervous system depression due to any cause, and blood dyscrasias. Contraindicated in individuals who have shown hypersensitivity to the drug. It is not known whether there is a cross-sensitivity between the thioxanthenes and the phenothiazine derivatives, but the possibility should be considered.

**Warnings:** *Tardive Dyskinesia*—Tardive dyskinesia, a syndrome consisting of potentially irreversible, involuntary, dyskinetic movements may develop in patients treated with neuroleptic (antipsychotic) drugs. Although the prevalence of the syndrome appears to be highest among the elderly, especially elderly women, it is impossible to rely upon prevalence estimates to predict, at the inception of neuroleptic treatment, which patients are likely to develop the syndrome. Whether neuroleptic drug products differ in their potential to cause tardive dyskinesia is unknown.

Both the risk of developing the syndrome and the likelihood that it will become irreversible are believed to increase as the duration of treatment and the total cumulative dose of neuroleptic drugs administered to the patient increase. However, the syndrome can develop, although much less commonly, after relatively brief treatment periods at low doses.

There is no known treatment for established cases of tardive dyskinesia, although the syndrome may remit, partially or completely, if neuroleptic treatment is withdrawn. Neuroleptic treatment, itself, however, may suppress (or partially suppress) the signs and symptoms of the syndrome and thereby may possibly mask the underlying disease process. The effect that symptomatic suppression has upon the long-term course of the syndrome is unknown

Given these considerations, neuroleptics should be prescribed in a manner that is most likely to minimize the occurrence of tardive dyskinesia. Chronic neuroleptic treatment should generally be reserved for patients who suffer from a chronic illness that, 1) is known to respond to neuroleptic drugs, and, 2) for whom alternative, equally effective, but potentially less harmful treatments are *not* available or appropriate. In patients who do require chronic treatment, the smallest dose and the shortest duration of treatment producing a satisfactory clinical response should be sought. The need for continued treatment should be reassessed periodically.

If signs and symptoms of tardive dyskinesia appear in a patient on neuroleptics, drug discontinuation should be considered. However, some patients may require treatment despite the presence of the syndrome.

(For further information about the description of tardive dyskinesia and its clinical detection, please refer to Information for Patients in the Precautions section, and to the Adverse Reactions section.)

*Neuroleptic Malignant Syndrome (NMS)*—A potentially fatal symptom complex sometimes referred to as Neuroleptic Malignant Syndrome (NMS) has been reported in association with antipsychotic drugs. Clinical manifestations of NMS are hyperpyrexia, muscle rigidity, altered mental status and evidence of autonomic instability (irregular pulse or blood pressure, tachycardia, diaphoresis, and cardiac dysrhythimas).

The diagnostic evaluation of patients with this syndrome is complicated. In arriving at a diagnosis, it is important to identify cases where the clinical presentation includes both serious medical illness (e.g., pneumonia, systemic infection, etc.) and untreated or inadequately treated extrapyramidal signs and symptoms (EPS). Other important considerations in the differential diagnosis include central anticholinergic toxicity, heat stroke, drug fever and primary central nervous system (CNS) pathology.

The management of NMS should include 1) immediate discontinuation of antipsychotic drugs and other drugs not essential to concurrent therapy, 2) intensive symptomatic treatment and medical monitoring, and 3) treatment of any concomitant serious medical problems for which specific treatments are available. There is no general agreement about specific pharmacological treatment regimens for uncomplicated NMS.

If a patient requires antipsychotic drug treatment after recovery from NMS, the potential reintroduction of drug therapy should be carefully considered. The patient should be carefully monitored, since recurrences of NMS have been reported.

*Usage in Pregnancy*—Safe use of Navane during pregnancy has not been established. Therefore, this drug should be given to pregnant patients only when, in the judgment of the physician, the expected benefits from the treatment exceed the possible risks to mother and fetus. Animal reproduction studies and clinical experience to date have not demonstrated any teratogenic effects.

In the animal reproduction studies with Navane, there was some decrease in conception rate and litter size, and an increase in resorption rate in rats and rabbits, changes which have been similarly reported with other psychotropic agents. After repeated oral administration of Navane to rats (5 to 15 mg/kg/day), rabbits (3 to 50 mg/kg/day), and monkeys (1 to 3 mg/kg/day) before and during gestation, no teratogenic effects were seen. (See Precautions.)

*Usage in Children*—The use of Navane in children under 12 years of age is not recommended because safety and efficacy in the pediatric age group have not been established.

As is true with many CNS drugs, Navane may impair the mental and/or physical abilities required for the performance of potentially hazardous tasks such as driving a car or operating machinery, especially during the first few days of therapy. Therefore, the patient should be cautioned accordingly.

As in the case of other CNS-acting drugs, patients receiving Navane should be cautioned about the possible additive effects (which may include hypotension) with CNS depressants and with alcohol.

**Precautions:** An antiemetic effect was observed in animal studies with Navane; since this effect may also occur in man, it is possible that Navane may mask signs of overdosage of toxic drugs and may obscure conditions such as intestinal obstruction and brain tumor.

In consideration of the known capability of Navane and certain other psychotropic drugs to precipitate convulsions, extreme caution should be used in patients with a history of convulsive disorders or those in a state of alcohol withdrawal since it may lower the convulsive threshold. Although Navane potentiates the actions of the barbiturates, the dosage of the anticonvulsant therapy should not be reduced when Navane is administered concurrently.

Caution as well as careful adjustment of the dosage is indicated when Navane is used in conjunction with other CNS depressants other than anticonvulsant drugs.

Though exhibiting rather weak anticholinergic properties, Navane should be used with caution in patients who are known or suspected to have glaucoma, or who might be exposed to extreme heat, or who are receiving atropine or related drugs.

Use with caution in patients with cardiovascular disease.

Also, careful observation should be made for pigmentary retinopathy, and lenticular pigmentation (fine lenticular pigmentation has been noted in a small number of patients treated with Navane for prolonged periods). Blood dyscrasias (agranulocytosis, pancytopenia, thrombocytopenic purpura), and liver damage (jaundice, biliary stasis) have been reported with related drugs.

Undue exposure to sunlight should be avoided. Photosensitive reactions have been reported in patients on Navane (thiothixene).

*Intramuscular Administration*—As with all intramuscular preparations, Navane Intramuscular should be injected well within the body of a relatively large muscle. The preferred sites are the upper outer quadrant of the buttock (i.e. gluteus maximus) and the mid-lateral thigh.

The deltoid area should be used only if well developed, such as in certain adults and older children, and then only with caution to avoid radial nerve injury. Intramuscular injections should not be made into the lower and mid-thirds of the upper arm. As with all intramuscular injections, aspiration is necessary to help avoid inadvertent injection into a blood vessel.

Neuroleptic drugs elevate prolactin levels; the elevation persists during chronic administration. Tissue culture experiments indicate that approximately one third of human breast cancers are prolactin-dependent *in vitro*, a factor of potential importance if the prescription of these drugs is contemplated in a patient with a previously detected breast cancer. Although disturbances such as galactorrhea, amenorrhea, gynecomastia, and impotence have been reported, the clinical significance of elevated serum prolactin levels is unknown for most patients. An increase in mammary neoplasms has been found in rodents after chronic administration of neuroleptic drugs. Neither clinical studies nor epidemiologic studies conducted to date, however, have shown an association between chronic administration of these drugs and mammary tumorigenesis; the available evidence is considered too limited to be conclusive at this time.

*Information for Patients*—Given the likelihood that some patients exposed chronically to neuroleptics will develop tardive dyskinesia, it is advised that all patients in whom chronic use is contemplated be given, if possible, full information about this risk. The decision to inform patients and/or their guardians must obviously take into account the clinical circumstances and the competency of the patient to understand the information provided.

**Adverse Reactions:** *Note:* Not all of the following adverse reactions have been reported with Navane (thiothixene). However, since Navane has certain chemical and pharmacologic similarities to the phenothiazines, all of the known side effects and toxicity associated with phenothiazine therapy should be borne in mind when Navane is used.

Cardiovascular effects: Tachycardia, hypotension, lightheadedness, and syncope. In the event hypotension occurs, epinephrine should not be used as a pressor agent since a paradoxical further lowering of blood pressure may result. Nonspecific EKG changes have been observed in some patients receiving Navane (thiothixene). These changes are usually reversible and frequently disappear on continued Navane therapy. The incidence of these changes is lower than that observed with some phenothiazines. The clinical significance of these changes is not known.

CNS effects: Drowsiness, usually mild, may occur although it usually subsides with continuation of Navane therapy. The incidence of sedation appears similar to that of the piperazine group of phenothiazines, but less than that of certain aliphatic phenothiazines. Restlessness, agitation and insomnia have been noted with Navane. Seizures and paradoxical exacerbation of psychotic symptoms have occurred with Navane infrequently.

Hyperreflexia has been reported in infants delivered from mothers having received structurally related drugs.

In addition, phenothiazine derivatives have been associated with cerebral edema and cerebrospinal fluid abnormalities.

Extrapyramidal symptoms, such as pseudo-parkinsonism, akathisia, and dystonia have been reported. Management of these extrapyramidal symptoms depends upon the type and severity. Rapid relief of acute symptoms may require the use of an injectable antiparkinson agent. More slowly emerging symptoms may be managed by reducing the dosage of Navane and/or administering an oral antiparkinson agent.

Persistent Tardive Dyskinesia: As with all antipsychotic agents tardive dyskinesia may appear in some patients on long-term therapy or may occur after drug therapy has been discontinued. The syndrome is characterized by rhythmical involuntary movements of the tongue, face, mouth or jaw (e.g., protrusion of tongue, puffing of cheeks, puckering of mouth, chewing movements). Sometimes these may be accompanied by involuntary movements of extremities.

Since early detection of tardive dyskinesia is important, patients should be monitored on an ongoing basis. It has been reported that fine vermicular movement of the tongue may be an early sign of the syndrome. If this or any other presentation of the syndrome is observed, the clinician should consider possible discontinuation of neuroleptic medication. (See Warnings section.)

Hepatic Effects: Elevations of serum transaminase and alkaline phosphatase, usually transient, have been infrequently observed in some patients. No clinically confirmed cases of jaundice attributable to Navane have been reported.

Hematologic Effects: As is true with certain other psychotropic drugs, leukopenia and leukocytosis, which are usually transient, can occur occasionally with Navane. Other antipsychotic drugs have been associated with agranulocytosis, eosinophilia, hemolytic anemia, thrombocytopenia and pancytopenia.

Allergic Reactions: Rash, pruritus, urticaria, photosensitivity and rare cases of anaphylaxis have been reported with Navane. Undue exposure to sunlight should be avoided. Although not experienced with Navane, exfoliative dermatitis and contact dermatitis (in nursing personnel) have been reported with certain phenothiazines.

Endocrine Disorders: Lactation, moderate breast enlargement and amenorrhea have occurred in a small percentage of females receiving Navane. If persistent, this may necessitate a reduction in dosage or the discontinuation of therapy. Phenothiazines have been associated with false positive pregnancy tests, gynecomastia, hypoglycemia, hyperglycemia, and glycosuria.

Autonomic Effects: Dry mouth, blurred vision, nasal congestion, constipation, increased sweating, increased salivation, and impotence have occurred infrequently with Navane therapy. Phenothiazines have been associated with miosis, mydriasis, and adynamic ileus.

Other Adverse Reactions: Hyperpyrexia, anorexia, nausea, vomiting, diarrhea, increase in appetite and weight, weakness or fatigue, polydipsia and peripheral edema.

Although not reported with Navane, evidence indicates there is a relationship between phenothiazine therapy and the occurrence of a systemic lupus erythematosus-like syndrome.

*Neuroleptic Malignant Syndrome (NMS): Please refer to the text regarding NMS in the WARNINGS section.*

NOTE: Sudden deaths have occasionally been reported in patients who have received certain phenothiazine derivatives. In some cases the cause of death was apparently cardiac arrest or asphyxia due to failure of the cough reflex. In others, the cause could not be determined nor could it be established that death was due to phenothiazine administration.

**Dosage:** Dosage of Navane should be individually adjusted depending on the chronicity and severity of the condition. See full prescribing information.

**Overdosage:** For information on signs and symptoms, and treatment of overdosage, see full prescribing information.

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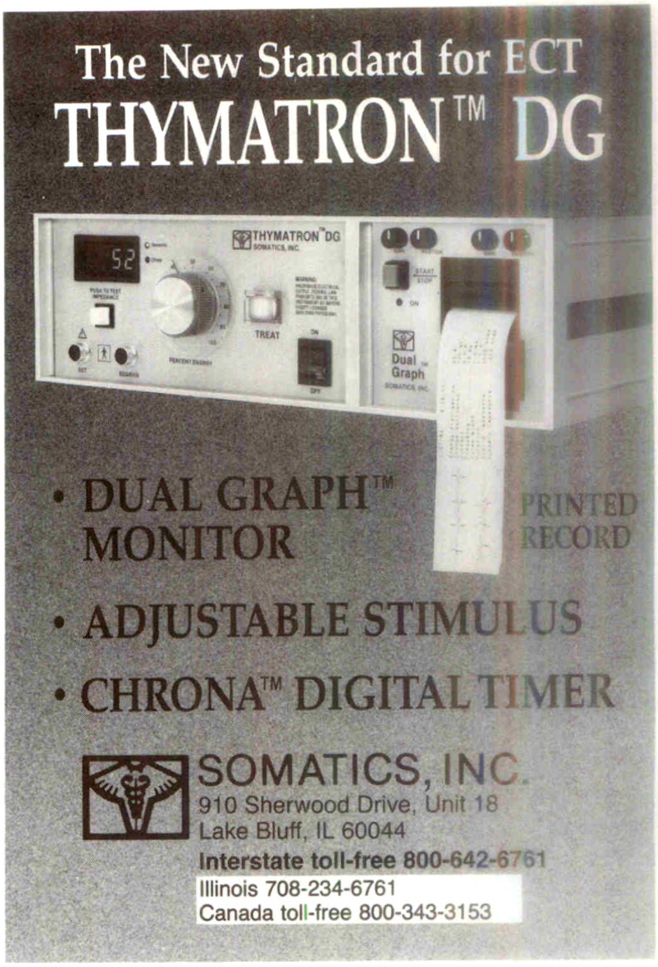

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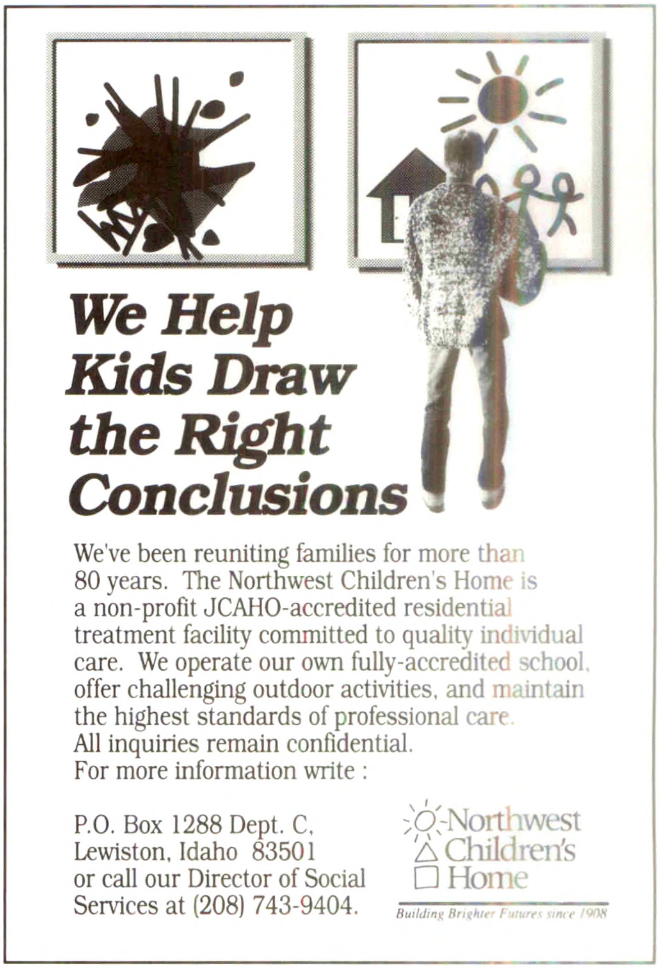

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March 1–3, "Non-Epileptic (Pseudoepileptic) Seizures," sponsored by the American Epilepsy Society and the Epilepsy Foundation of America, Fort Lauderdale, Florida. Contact Mrs. Linda Tuchman, Neurology Service (127), VAMC, 130 West Kingsbridge Road, The Bronx, NY 10468; 212-584-9000, ext. 1885.

March 6–9, 8th Annual Symposium in Forensic Psychiatry, American College of Forensic Psychiatry, Las Vegas. Contact Ed Miller, Executive Director, 26701 Quail Creek, Suite 295, Laguna Hills, CA 92656; 714-831-0236.

March 7, annual meeting, Association for Academic Psychiatry, Seattle. Contact Mary O'Loughlin, Department of Psychiatry, Mount Auburn Hospital, Cambridge, MA 02238; 617-492-3500, ext. 4314.

March 7–10, 2nd International Congress on Somatotherapy, Punta del Este, Uruguay. Contact Luis Franco, 4969/2 Montevideo, Uruguay.

March 19–21, Consensus Development Conference on Surgery for Epilepsy, National Institute of Neurological Disorders and Stroke and the Office of Medical Applications of Research, National Institutes of Health, Bethesda, Maryland. Contact Conference Registrar, Prospect Associates, Suite 500, 1801 Rockville Pike, Rockville, MD 20852; 301-468-MEET.

March 22–24, 17th Annual Conference on Dyslexia, New York branch of the Orton Dyslexia Society, Inc., New York. Contact the New York branch of the Orton Dyslexia Society, 80 Fifth Avenue, New York, NY 10011; 212-691-1930.

March 28–April 1, 18th Annual Meeting of the American Society for Psychosomatic Obstetrics and Gynecology, New York. Contact Patricia D. Stahr, Administrator, Liaison Activities, The American College of Obstetricians and Gynecologists, 409 12th Street, SW, Washington, DC 20024-2188; 202-863-2514.

## APRIL

April 1–6, 6th World Congress on Pain, Norwood, South Australia. Contact Elliservice Convention Management, P.O. Box 753, Norwood, South Australia 5067; 08-332-4068 or 08-31-5687.

April 4–6, International Symposium on New Concepts in Anxiety, Castres, France. Contact Martine Dehaye, Centre de Recherche Pierre Fabre, 17 avenue Jean Moulin, 81100 Castres, France; 63-35-56-07.

April 11–14, Asian Medicine: Past, Present and Future (Mental Health Care and Methods, Use of Medicinal Plants, Concepts and Applications of Acupuncture, and Other Alternative General Medical Practices), Bangkok, Thailand. Contact Ann McCormick, Southern California Neuropsychiatric Institute, 6794 La Jolla Blvd, La Jolla, CA 92037; 619-454-2102.

April 19–21, 31st National Student Research Forum, University of Texas Medical Branch, Galveston, Texas. Contact National Student Research Forum, Room 209, Family Medicine Building, Route H-56, University of Texas Medical Branch, Galveston, TX 77550; 409-761-3762.

April 22–May 5, 2nd International Colloquium on Advances in Intensive Psychotherapy, Jerusalem. Contact David Fogel, M.D., 200 Fisher Building, Detroit, MI 48202.

April 24–27, 36th Annual Meeting of the American Society for Artificial Internal Organs, Washington, DC. Contact ASAIO, P.O. Box C, Boca Raton, FL 33429; 407-391-8589.

April 25–27, 1st International Congress of Movement Disorders, Washington, D.C. Contact Mark Hallett, M.D., Scientific Secretariat, National Institute of Neurologic Disorders and Stroke, National Institutes of Health, Building 10, Room 5N226, Bethesda, MD 20892; or Secretariat ISMD, P.O. Box CH-4005, Basel, Switzerland.

April 27–29, 4th International Conference on Eating Disorders, New York. Contact Eric Schwartz, Program Administrator, Office of Continuing Medical Education, Albert Einstein College of Medicine/Montefiore Medical Center, 3301 Bainbridge Avenue, Bronx, New York 10467; 212-920-6674.

April 29–May 1, 2nd International United Arab Emirates Conference of Psychiatry, Abu Dhabi, United Arab Emirates. Contact Dr. Rafia Ghubash, c/o Dr. Hassan Abd El Rahman,

*(Continued on page A47)*

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**Precautions:** Use in schizophrenic patients may result in an exacerbation of the psychosis or may activate latent schizophrenic symptoms; in overactive or agitated patients, increased anxiety and agitation may occur; in manic-depressive patients, symptoms of the manic phase may emerge. Administration of reserpine during therapy with a tricyclic antidepressant has been shown to produce a "stimulating" effect in some depressed patients. Troublesome patient hostility may be aroused. Epileptiform seizures may accompany administration. Close supervision and careful adjustment of dosage are required when used with other anticholinergic drugs and sympathomimetic drugs. Concurrent administration of cimetidine can produce clinically significant increases in the plasma concentrations of the tricyclic antidepressant. Patients should be informed that the response to alcohol may be exaggerated. When essential, may be administered with electroconvulsive therapy, although the hazards may be increased. Discontinue the drug for several days, if possible, prior to elective surgery. The possibility of a suicidal attempt by a depressed patient remains after the initiation of treatment; in this regard, it is important that the least possible quantity of drug be dispensed at any given time. Both elevation and lowering of blood sugar levels have been reported.

A case of significant hypoglycemia has been reported in a type II diabetic patient maintained on chlorpropamide (250 mg/day), after the addition of nortriptyline (125 mg/day).

**Adverse Reactions:** *Cardiovascular*—Hypotension, hypertension, tachycardia, palpitation, myocardial infarction, arrhythmias, heart block, stroke. *Psychiatric*—Confusional states (especially in the elderly) with hallucinations, disorientation, delusions; anxiety, restlessness, agitation; insomnia, panic, nightmares; hypomania; exacerbation of psychosis. *Neurologic*—Numbness, tingling, paresthesias of extremities; incoordination, ataxia, tremors; peripheral neuropathy; extrapyramidal symptoms; seizures, alteration in EEG patterns; tinnitus. *Anticholinergic*—Dry mouth and, rarely, associated sublingual adenitis; blurred vision, disturbance of accommodation, mydriasis; constipation, paralytic ileus; urinary retention, delayed micturition, dilation of the urinary tract. *Allergic*—Skin rash, petechiae, urticaria, itching, photosensitization (avoid excessive exposure to sunlight); edema (general or of face and tongue), drug fever, cross-sensitivity with other tricyclic drugs. *Hematologic*—Bone marrow depression, including agranulocytosis; eosinophilia; purpura; thrombocytopenia. *Gastrointestinal*—Nausea and vomiting, anorexia, epigastric distress, diarrhea, peculiar taste, stomatitis, abdominal cramps, black-tongue. *Endocrine*—Gynecomastia in the male, breast enlargement and galactorrhea in the female; increased or decreased libido, impotence; testicular swelling; elevation or depression of blood sugar levels; syndrome of inappropriate ADH (antidiuretic hormone) secretion. *Other*—Jaundice (simulating obstructive), altered liver function; weight gain or loss; perspiration; flushing; urinary frequency, nocturia; drowsiness, dizziness, weakness, fatigue; headache; parotid swelling; alopecia. *Withdrawal Symptoms*—Though these are not indicative of addiction, abrupt cessation of treatment after prolonged therapy may produce nausea, headache, and malaise.

**Overdosage:** Toxic overdosage may result in confusion, restlessness, agitation, vomiting, hyperpyrexia, muscle rigidity, hyperactive reflexes, tachycardia, ECG evidence of impaired conduction, shock, congestive heart failure, stupor, coma, and CNS stimulation with convulsions followed by respiratory depression. Deaths have occurred with drugs of this class. No specific antidote is known; general supportive measures are indicated, with gastric lavage. [PAM-Z17—1/13/89]

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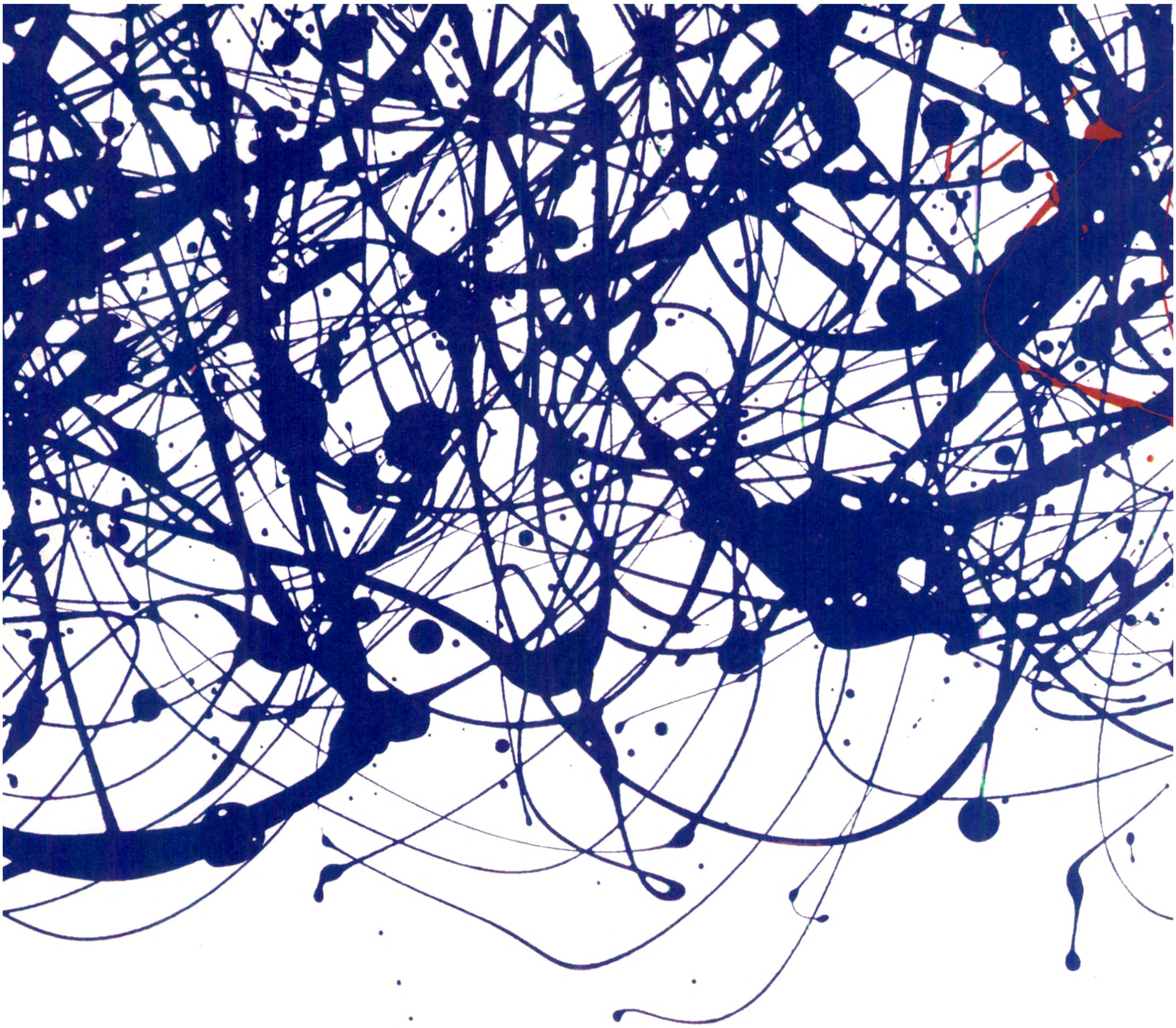


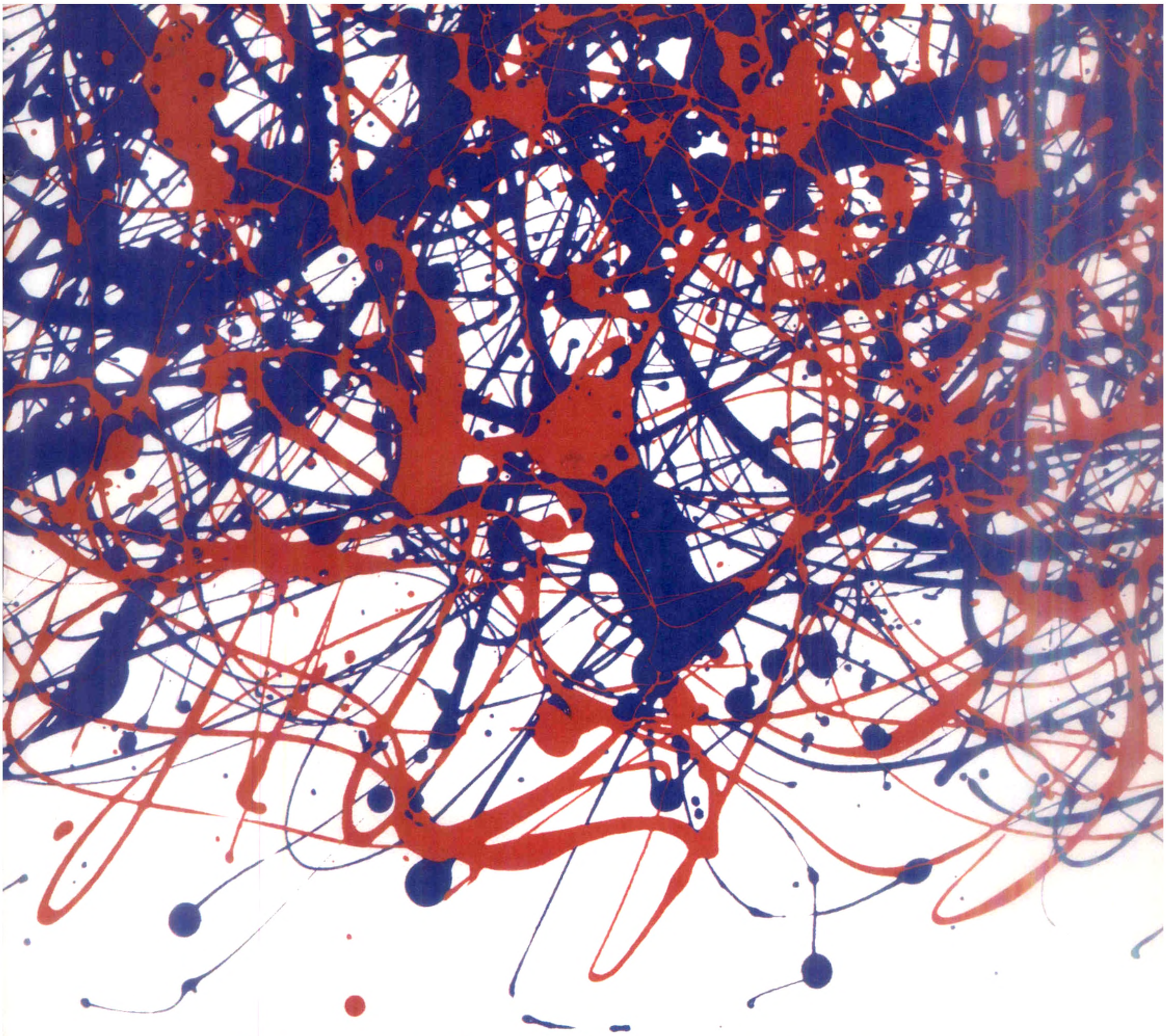
# With depression . .

In a clinical trial, XANAX was effective in reducing anxiety symptoms associated with moderate to severe depression.*

Patients taking XANAX should be alerted to possible additive CNS depressant effects when it is administered with other medications that produce CNS depression.

The usual starting dosage of XANAX is 0.25 to 0.5 mg t.i.d.

*Data on file, The Upjohn Company



you often find anxiety

TABLETS 0.5 MG

**Xanax**®

alprazolam Ⓘⓥ

**For anxiety associated with depression**

**Upjohn** Please see adjacent page for brief summary of prescribing information.

The Upjohn Company
Kalamazoo, Michigan 49001, USA

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**XANAX® Tablets**
**(alprazolam, Ⓒ)**

**INDICATIONS AND USAGE**
Anxiety disorders, short-term relief of the symptoms of anxiety, and anxiety associated with depression. Anxiety or tension associated with the stress of everyday life usually does not require an anxiolytic. Effectiveness for more than four months has not been established; periodically reassess the usefulness of the drug for the individual patient.

**CONTRAINDICATIONS**
Sensitivity to XANAX or other benzodiazepines, and in acute narrow angle glaucoma.

**WARNINGS**
XANAX is not of value in treating psychosis and should not be used in lieu of appropriate treatment. Patients receiving XANAX should be cautioned about hazardous occupations or activities requiring full alertness and also about simultaneous ingestion of alcohol or other CNS depressants.

Benzodiazepines can cause fetal harm in pregnant women, hence women who may become pregnant should be warned. Avoid during the first trimester. Withdrawal seizures have been reported upon rapid dose reduction or abrupt discontinuation, thus reduce dose gradually. (See Drug Abuse and Dependence and Dosage and Administration.)

**PRECAUTIONS**
***General:*** If XANAX is combined with other psychotropics or anticonvulsants, consider drug potentiation. (See Drug Interactions.) Use the usual precautions in patients with renal or hepatic impairment and regarding prescription size in depressed and suicidal patients. In elderly and debilitated patients, use the lowest possible dose. (See Dosage and Administration.) Hypomania and mania has been reported in depressed patients.

***Information for Patients:*** Alert patients about: (a) consumption of alcohol and drugs, (b) possible fetal abnormalities, (c) operating machinery or driving, (d) not increasing dose of the drug due to risk of dependence, (e) not stopping the drug abruptly. *Laboratory Tests:* Not ordinarily required in otherwise healthy patients. *Drug Interactions:* Additive CNS depressant effects with other psychotropics, anticonvulsants, antihistamines, ethanol and other CNS depressants. Plasma levels of imipramine and desipramine are increased. Pharmacokinetic interactions with other drugs have been reported. Cimetidine can delay clearance of benzodiazepines. *Drug/Laboratory Test Interactions:* No consistent pattern for a drug or test. *Carcinogenesis, Mutagenesis, Impairment of Fertility:* No carcinogenic potential or impairment of fertility in rats. *Pregnancy:* See Warnings. *Nonteratogenic Effects:* The child born of a mother on benzodiazepines may be at some risk for withdrawal symptoms, neonatal flaccidity and respiratory problems. *Labor and Delivery:* No established use. *Nursing Mothers:* Benzodiazepines are excreted in human milk. Women on XANAX should not nurse. *Pediatric Use:* Safety and effectiveness in children below the age of 18 have not been established.

**ADVERSE REACTIONS**
Side effects are generally observed at the beginning of therapy and usually disappear with continued medication. In the usual patient, the most frequent side effects are likely to be an extension of the pharmacologic activity of XANAX, e.g., drowsiness or lightheadedness.

*Central nervous system:* Drowsiness, lightheadedness, depression, headache, confusion, insomnia, nervousness, syncope, dizziness, akathisia, and tiredness/sleepiness. *Gastrointestinal:* Dry mouth, constipation, diarrhea, nausea/vomiting, and increased salivation. *Cardiovascular:* Tachycardia/palpitations, and hypotension. *Sensory:* Blurred vision. *Musculoskeletal:* Rigidity and tremor. *Cutaneous:* Dermatitis/allergy. *Other side effects:* Nasal congestion, weight gain, and weight loss.

Withdrawal seizures with rapid decrease or abrupt discontinuation. (See Warnings.)

The following adverse events have been reported with benzodiazepines: dystonia, irritability, concentration difficulties, anorexia, transient amnesia or memory impairment, loss of coordination, fatigue, seizures, sedation, slurred speech, jaundice, musculoskeletal weakness, pruritus, diplopia, dysarthria, changes in libido, menstrual irregularities, incontinence, and urinary retention.

Paradoxical reactions such as stimulation, agitation, rage, increased muscle spasticity, sleep disturbances, and hallucinations may occur. Should these occur, discontinue the drug.

During prolonged treatment, periodic blood counts, urinalysis, and blood chemistry analysis are advisable. Minor EEG changes, of unknown significance, have been observed.

Liver enzyme elevations, gynecomastia and galactorrhea have been reported but no causal relationship was established.

**DRUG ABUSE AND DEPENDENCE**
*Physical and Psychological Dependence:* Withdrawal symptoms including seizures have occurred following abrupt discontinuance or rapid dose reduction of benzodiazepines. (See Warnings.) Dosage should be gradually tapered under close supervision. Patients with a history of seizures or epilepsy should not be abruptly withdrawn from XANAX. Addiction-prone individuals should be under careful surveillance. *Controlled Substance Class:* XANAX is a controlled substance and has been assigned to schedule IV.

**OVERDOSAGE**
Manifestations include somnolence, confusion, impaired coordination, diminished reflexes and coma. No delayed reactions have been reported.

**DOSAGE AND ADMINISTRATION**
Dosage should be individualized.

The usual starting dose is 0.25 to 0.5 mg, t.i.d. Maximum total daily dose is 4 mg. In the elderly or debilitated, the usual starting dose is 0.25 mg, two or three times daily. Reduce dosage gradually when terminating therapy, by no more than 0.5 mg every three days.

**HOW SUPPLIED**
XANAX Tablets are available as 0.25 mg, 0.5 mg, and 1 mg tablets.

**CAUTION:** FEDERAL LAW PROHIBITS DISPENSING WITHOUT PRESCRIPTION.

B-8-S
J-2252
November, 1989

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The American Psychiatric Association (APA) is pleased to announce the funding of the Program for Minority Research Training in Psychiatry by the National Institute of Mental Health (NIMH). This program will sponsor training of minority medical students, psychiatric residents, and fellows who are interested in research by providing advice, placement assistance, stipends, travel, and other expenses.

For further information about the Program for Minority Research Training in Psychiatry, call or write Harold Alan Pincus, M.D., or Jeanne Spurlock, M.D., at the American Psychiatric Association, 1400 K Street, N.W., Washington, D.C. 20005; Telephone 202-682-6238; or FAX 202-682-6114.

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Psychiatry Today

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# BREAKTHROUGH

## FOR THOUSANDS OF PROBLEM SCHIZOPHRENIC PATIENTS AND THEIR PSYCHIATRISTS

## Sandoz Introduces CLOZARIL® (clozapine) — A Breakthrough Antipsychotic Agent

### For Patients Who Fail to Respond Adequately to Treatment With Appropriate Courses of Standard Antipsychotic Drugs

Sandoz Pharmaceuticals Corporation has announced the introduction of CLOZARIL (clozapine), a new, atypical antipsychotic agent that has demonstrated efficacy against symptoms of schizophrenia in severely ill ("problem") patients who fail to respond adequately to treatment with appropriate courses of standard antipsychotic drugs. The drug, whose pharmacologic profile suggests a unique mode of action, is being hailed as the first breakthrough in antipsychotic therapy in more than two decades. In a clinical trial, as reported by John Kane, MD, and others in an original article published in *Archives of General Psychiatry*, September 1988, CLOZARIL (clozapine) proved significantly more effective than chlorpromazine in controlling both the positive and negative symptoms of chronic schizophrenia.

"CLOZARIL poses a very exciting opportunity," said John Kane, MD, chairman of the department of psychiatry, Hillside Hospital–Long Island Jewish Medical Center, and a key CLOZARIL investigator. "Our multicenter study suggests that the drug may be an important therapeutic advance in the treatment of schizophrenia." Other investigators have reported similar successes with CLOZARIL (clozapine) in many severely ill ("problem") schizophrenics who failed to respond adequately to treatment with

*(Continued on page 3)*

## Haloperidol Failures Respond

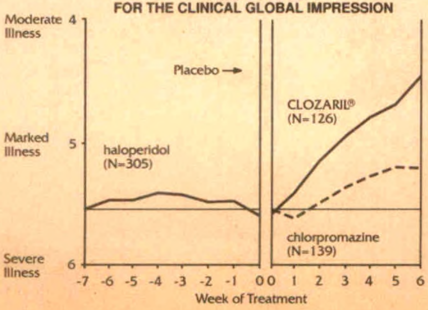
Chronic schizophrenics who had failed to respond to a six-week course of haloperidol showed significant improvement with CLOZARIL® therapy in the landmark multicenter clinical trial. Symptoms began to improve within two weeks after CLOZARIL therapy was begun. Improvement continued throughout the course of the study.

Study subjects were selected on the basis of a history of failure to respond to standard antipsychotic therapy. Prospective criteria included treatment failure on at least 60 mg/day of haloperidol. After six weeks, only 1.6% of the patients treated with haloperidol had responded positively. Others failed to respond or were not able to tolerate the drug.

When treated with CLOZARIL (clozapine), haloperidol nonresponders demonstrated significant improvement in a broad range of symptoms on the Brief Psychiatric Rating Scale (BPRS), including the positive symptom cluster of thought disturbances: hallucinations, unusual thought content, grandiosity and conceptual disorganization. Many CLOZARIL-treated patients were rated significantly improved in the negative symptom cluster of anergia. The initial response to CLOZARIL therapy was dramatic and achieved statistical significance after only two weeks of treatment.

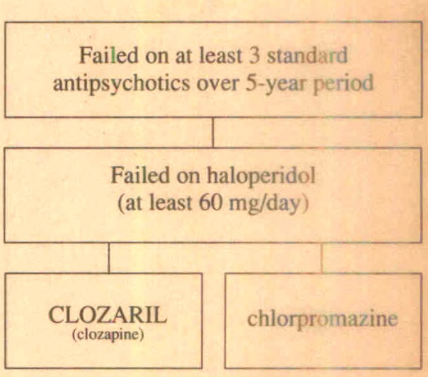
Researchers concluded that some 30% of CLOZARIL-treated patients showed significant improvement in overall clinical condition in only six weeks. Similar results were seen in only 4% of chlorpromazine-treated patients. ■

MEAN SCORES
FOR THE CLINICAL GLOBAL IMPRESSION



## Rigorous Study Shows Superior Efficacy

In a landmark U.S. multicenter trial, CLOZARIL® (clozapine) proved to have greater efficacy than chlorpromazine in problem schizophrenics who had previously failed on haloperidol.


Failed on at least 3 standard antipsychotics over 5-year period
Failed on haloperidol (at least 60 mg/day)
CLOZARIL (clozapine)
chlorpromazine

According to Dr. Kane, the unusual protocol of the CLOZARIL trial had few precedents. "Many people thought this was an inordinately conservative test that really stacked the deck against clozapine," the investigator said.

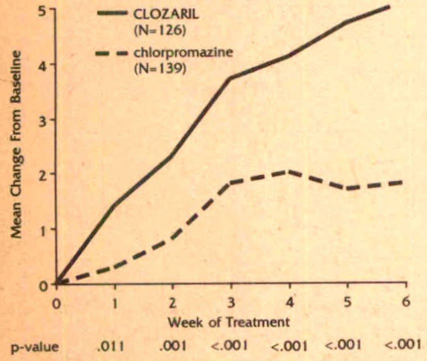
Patients were first selected on the basis of a history of failure to respond to at least three drugs from two antipsychotic classes over the previous five years. They were then treated with at least 60 mg/day of haloperidol and 6 mg/day of benztropine for up to six weeks. Patients who failed to respond were randomized into two groups — one treated with CLOZARIL (clozapine) and one with chlorpromazine plus benztropine. Prophylactic benztropine was employed in the chlorpromazine group to mask extrapyramidal side effects and help maintain double-blind conditions. In this population of haloperidol failures, CLOZARIL (clozapine) demonstrated significant superiority over chlorpromazine in the treatment of positive and negative schizophrenic symptoms. ■

# Positive and Negative Sym
# Respond to CLOZARIL® (c

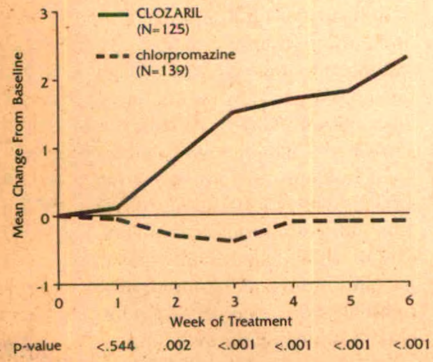
Dramatic evidence from a double-blind multicenter U.S. trial, published in the *Archives of General Psychiatry*, September 1988, indicates that CLOZARIL (clozapine) is effective against both "positive" and "negative" symptoms of schizophrenia in severely ill ("problem") patients who failed to respond adequately to treatment with appropriate courses of standard antipsychotic drugs. Within the first two weeks of CLOZARIL treatment, patients improved in several key areas of positive or florid symptomatology as measured on the Brief Psychiatric Rating Scale (BPRS): conceptual disorganization, suspiciousness, hallucinatory behavior, unusual thought content. CLOZARIL patients showed substantial improvement earlier and to a far greater degree than control patients treated with chlorpromazine.

Although the positive symptoms of schizophrenia have traditionally received the most clinical attention, there is growing

**BRIEF PSYCHIATRIC RATING SCALE**
**CLUSTER OF FOUR**
**POSITIVE SYMPTOMS**
(conceptual disorganization,
suspiciousness, hallucinatory behavior,
unusual thought content)



**BRIEF PSYCHIATRIC RATING SCALE**
**ANERGIA FACTOR**



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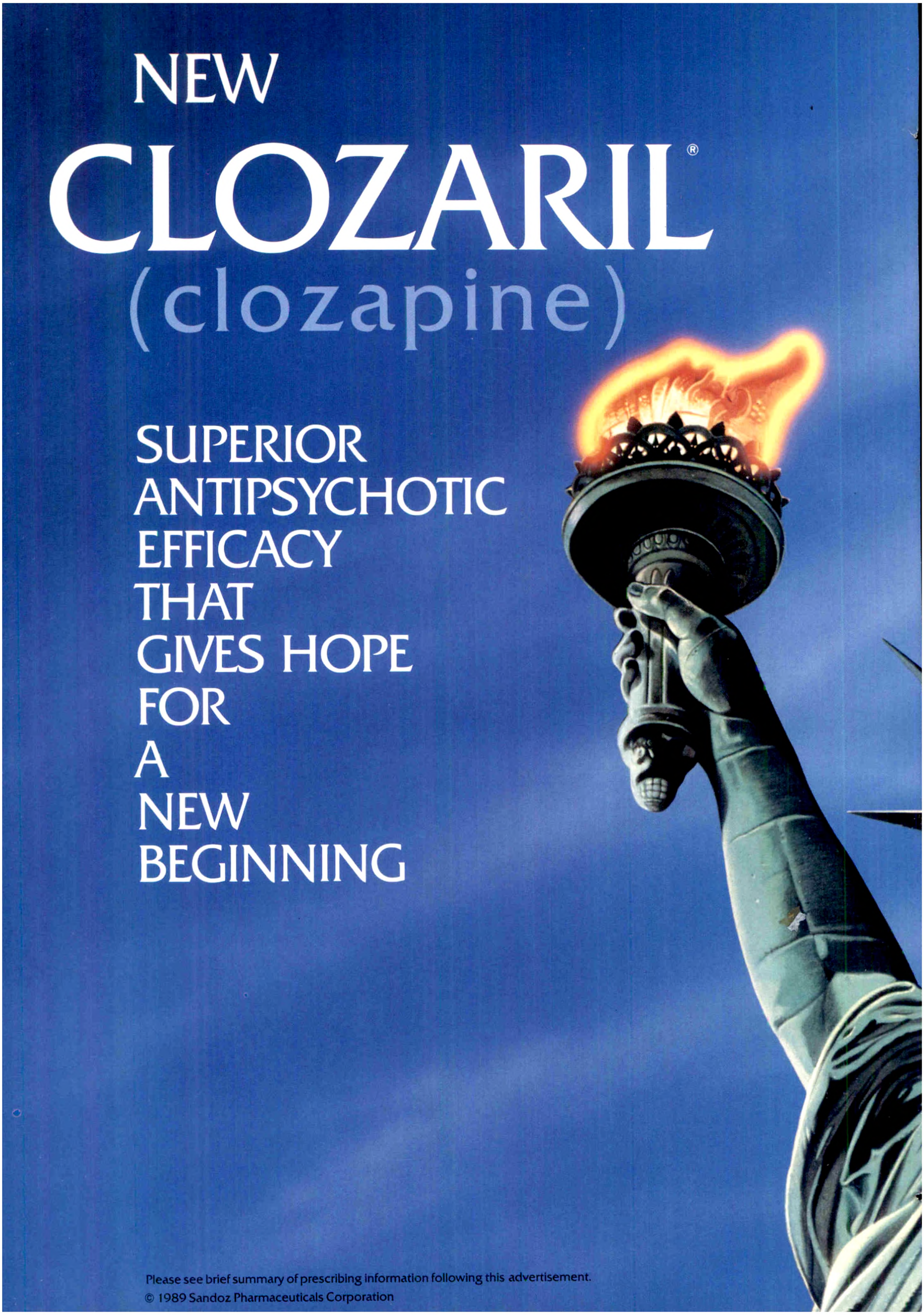
NTRODUCING

# A BEACON OF
# HOPE

FOR THOUSANDS
PROBLEM SCHIZOPHRENIC
PATIENTS
ND THEIR PSYCHIATRISTS



NEW

CLOZARIL®

(clozapine)

SUPERIOR
ANTIPSYCHOTIC
EFFICACY
THAT
GIVES HOPE
FOR
A
NEW
BEGINNING

Please see brief summary of prescribing information following this advertisement.

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## HOPE BEGINS WITH SUPERIOR SYMPTOMATIC CONTROL*

In a six-week controlled study in severely ill ("problem") schizophrenic patients who failed to respond adequately to treatment with appropriate courses of standard antipsychotic drugs:

- CLOZARIL® (clozapine) succeeded after standard antipsychotics, including haloperidol, failed
- Thirty percent of CLOZARIL patients experienced dramatic global improvement in only six weeks (as determined by the study's rigorous efficacy criteria) vs only 4% of patients receiving chlorpromazine
- Efficacy in both positive and negative symptomatology

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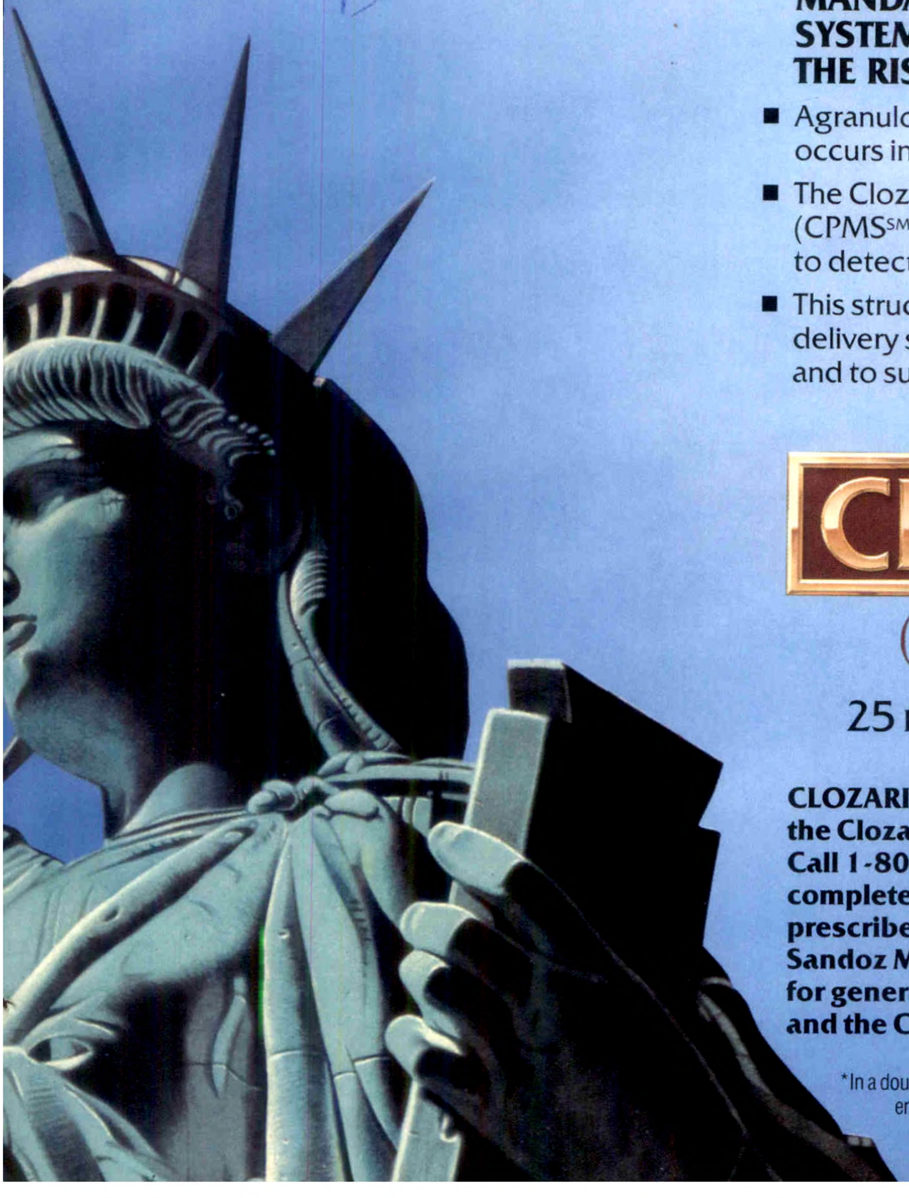

## HOPE CONTINUES WITH A VIRTUAL ABSENCE OF CERTAIN ACUTE EXTRAPYRAMIDAL SYMPTOMS

- CLOZARIL® (clozapine) is indicated for patients intolerant of standard antipsychotics
- No confirmed cases of tardive dyskinesia in over 15 years' worldwide experience
- Side effects that have been reported include: agranulocytosis (1–2%), transient sedation (39%), hypersalivation (31%), tachycardia (25%), constipation (14%), hypotension (9%), hypertension (4%) and weight gain (4%)[†]
- CLOZARIL use is associated with a substantial risk of seizure, an apparently dose-dependent reaction affecting 1–2% of patients at low doses (below 300 mg/day), 3–4% at moderate doses, and 5% at high doses (600–900 mg/day)[‡]

## HOPE IS MAINTAINED THROUGH A MANDATORY WBC MONITORING SYSTEM WHICH HELPS MANAGE THE RISK OF AGRANULOCYTOSIS

- Agranulocytosis, a potentially fatal disorder, occurs in 1–2% of patients
- The Clozaril Patient Management System℠ (CPMS℠) was created as an efficient means to detect developing agranulocytosis
- This structured weekly monitoring and drug delivery system helps to protect the patient and to support the physician

# CLOZARIL®

(clozapine)

25 mg and 100 mg tablets

**CLOZARIL therapy is available only through the Clozaril Patient Management System. Call 1-800-237-CPMS (2767) or mail in a completed CPMS patient enrollment form to prescribe CLOZARIL (clozapine). Contact your Sandoz Mental Health Sales Representative for general information on CLOZARIL (clozapine) and the Clozaril Patient Management System.**

*In a double-blind study of CLOZARIL (clozapine) versus chlorpromazine encompassing 268 patients, all of whom had first failed on at least three standard antipsychotics over a five-year period and then on a trial of high-dose haloperidol.

INTRODUCING

# CLOZARIL®

## (clozapine)

## A BEACON OF HOPE FOR PROBLEM SCHIZOPHRENIC PATIENTS

**To prescribe**
**CLOZARIL**
**(clozapine)**
**call 1-800-237-CPMS (2767)**
**or mail in a completed CPMS patient enrollment form.**

†Tachycardia, hypotension and hypertension are the principal cardiovascular effects associated with CLOZARIL (clozapine).

‡Because of the substantial risk of seizure associated with CLOZARIL use, a dosage ceiling of 600 mg/day is recommended, although some patients may require up to 900 mg/day for a therapeutic effect.

HOPE
FOR A NEW BEGINNING

CLOZARIL®
(clozapine)
25 mg and 100 mg tablets

**SANDOZ**PHARMACEUTICALS
Corporation, E. Hanover, NJ 07936 (201) 503-7500

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# BREAKTHROUGH

*(Continued from page 1)*

appropriate courses of standard antipsychotic drugs. Herbert Meltzer, MD, Douglas Danford Bond Professor of Psychiatry at Case Western Reserve University School of Medicine, demonstrated the effect of 6–9 months' treatment with CLOZARIL® (clozapine) on social function and interpersonal relationships in 21 problem schizophrenic patients. According to Dr. Meltzer, "The extent of improvement in the QLS [Quality of Life Scale] scores after 6 months' clozapine treatment was impressive. Total QLS scores nearly tripled during this period. Total QLS scores at least doubled in 76% of the patients. The improvement was most marked in the area of ability to work or return to school, but was also strong in intrapsychic foundations and interpersonal relations."

The new drug has created considerable excitement among families of chronic schizophrenic patients. As one parent said, "For us, CLOZARIL (clozapine) means new hope, and that's been a scarce commodity among schizophrenic patients and their families."

Because of its unique pharmacologic profile, CLOZARIL (clozapine) is thought to have a somewhat different mode of action than standard antipsychotics. The new drug is characterized by a virtual absence of certain acute extrapyramidal symptoms (e.g., dystonia). Also, unlike standard antipsychotics, it causes little or no elevation in serum prolactin levels and has not been linked to any confirmed cases of tardive dyskinesia.

However, it does carry an increased risk of seizure and agranulocytosis, necessitating weekly blood monitoring for all patients. The incidence of agranulocytosis, a potentially fatal disorder, associated with CLOZARIL (clozapine) is 1–2%. In Europe — principally before 1977 — prior to recognition and management of the risk, a number of fatalities occurred. With mandatory weekly white blood cell (WBC) monitoring, all cases in the United States through mid-1989 (15 in over 1,700 patients) have reversed, and no fatalities have occurred. ■

## Temple University Accredits CLOZARIL® Educational Program

Temple University has accredited the CLOZARIL Educational Program developed by Sandoz Pharmaceuticals Corporation to ensure safe and efficacious use of this new atypical antipsychotic agent. A series of teleconference workshops will be held at over 600 sites across the country. Physicians who participate will receive 4 hours of CME credit for attending the conference and completing the self-study materials.

These regional workshops will feature videotaped presentations and live interactive discussions via two-way telephone hookups. This will allow CLOZARIL investigators and other experts to answer audience questions on the spot. Psychiatrists and allied healthcare professionals attending the workshops will receive information about the benefits and risks of CLOZARIL therapy and the appropriate selection and management of patients.

Comprehensive take-home materials will include prescribing and product information, a psychiatrist's guide to CLOZARIL-associated agranulocytosis and a detailed description of the Clozaril Patient Management System$^{SM}$ (CPMS$^{SM}$). ■

## Side Effects Profile Further Distinguishes CLOZARIL® (clozapine)

Because of its unique pharmacologic profile, CLOZARIL (clozapine) appears to have a more specific mechanism of action than standard antipsychotics. This may be the reason for the virtual absence of certain acute extrapyramidal side effects — and no confirmed cases of tardive dyskinesia. Researchers theorize that this is because the drug has been shown in animal studies to be more selective for dopamine receptors in the limbic area of the brain, rather than the striatal receptors affected by most standard antipsychotics. In addition, in both preclinical and clinical studies, CLOZARIL (clozapine) causes little or no elevation of serum prolactin levels, and thus tends not to produce prolactin-related side effects as do other antipsychotic drugs.

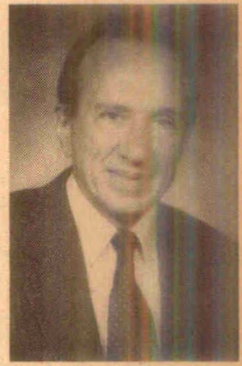
CLOZARIL (clozapine) is, however, associated with a higher incidence of agranulocytosis than standard antipsychotics — 1–2% as compared with 0.1% for standard agents. Careful monitoring through the Clozaril Patient Management System$^{SM}$ (CPMS$^{SM}$) will help promote early detection and timely drug discontinuation. Other side effects that have been reported include transient sedation (39%), hypersalivation (31%), tachycardia (25%), constipation (14%), hypotension (9%), seizures (5%), hypertension (4%) and weight gain (4%).

CLOZARIL use is associated with a substantial risk of seizure, an apparently dose-dependent reaction affecting 1–2% of patients at low doses (below 300 mg/day), 3–4% at moderate doses, and 5% at high doses (600–900 mg/day). In the multicenter

*(Continued on page 4)*

## CLOZARIL® Researcher Recounts CLOZARIL History

"I've seen CLOZARIL (clozapine) through its ups and downs," said Gilbert Honigfeld, PhD, associate director of Sandoz Research Institute, who has piloted the drug's development since joining Sandoz in 1973. Honigfeld recounted how the drug was first discovered in 1960 by Swiss scientists at the Wander Division of Sandoz and was being used in Europe in the 1970s when reports of agranulocytosis appeared.



These reports led to cessation of active U.S. CLOZARIL research for a number of years. "But clinicians would not let go of it," Honigfeld recalled. Patients were given the drug on a compassionate need basis, and evidence continued to mount that not only did CLOZARIL (clozapine) have superior efficacy, but that the risk of agranulocytosis could be managed with careful monitoring. Sandoz resumed clinical R&D in the '80s, and submitted results of its rigorous study in severely ill schizophrenic patients to government health officials in August 1987. ■

## Reimbursement

Efforts are being made to ensure that the majority of patients selected for CLOZARIL® therapy will be eligible to have their Clozaril Patient Management System$^{SM}$ (CPMS$^{SM}$) costs reimbursed by third-party payers, such as state Medicaid programs and the Veterans Administration. Additionally, duration of hospitalization is expected to decrease for patients on CLOZARIL therapy. In one retrospective study, the time spent outside institutions increased from 44% before CLOZARIL treatment to 63% in the second year of treatment with CLOZARIL (clozapine). That results in significant savings in cost of care as former inpatients become outpatients. Around the country, enthusiasm is being expressed for the new medication, which is expected to reduce substantially the chronic care costs of schizophrenia in a limited patient population. ■

# Patient Management System a Success

Early detection is the key to safe management of CLOZARIL®-induced agranulocytosis. Clinicians are expressing approval of the new Clozaril Patient Management System$^{SM}$ (CPMS$^{SM}$), a comprehensive system of WBC testing, pharmacy, clinical laboratory and drug distribution services, all linked to compliance with required safety monitoring. The program has been tested in pilot studies across the U.S. and has achieved over 99% blood monitoring compliance on the part of the patients — without interfering with the physician's medical control.

The system is designed to detect falling WBC counts that may be indicative of impending agranulocytosis. In the event of abnormal test results, the physician will be notified immediately. If the abnormal test shows only a downward trend from a normal WBC count to a count that has not yet reached leukopenia, additional blood work, such as a complete blood count and a differential count, should be performed. If the WBC count stabilizes, the patient returns to the normal cycle of weekly monitoring.

*Patients who are discontinued from CLOZARIL (clozapine) because of severe leukopenia or agranulocytosis cannot resume therapy.* A single national database is maintained by CPMS in an effort to ensure that any patient who develops severe leukopenia or agranulocytosis is not rechallenged with CLOZARIL (clozapine).

Caremark Homecare, Inc., a national home healthcare agency, has been chosen to implement the system. CPMS Case Administrators arrange for patients' blood to be drawn weekly, and the samples sent for analysis to Roche Biomedical Laboratories, a national clinical laboratory. A Clozapak™ seven-day supply of CLOZARIL (clozapine) is released upon collection of blood samples. CPMS operates on the principle of "No blood, no drug" to ensure that CLOZARIL (clozapine) is administered in the safest possible manner. The drug will be obtainable only through the Clozaril Patient Management System.

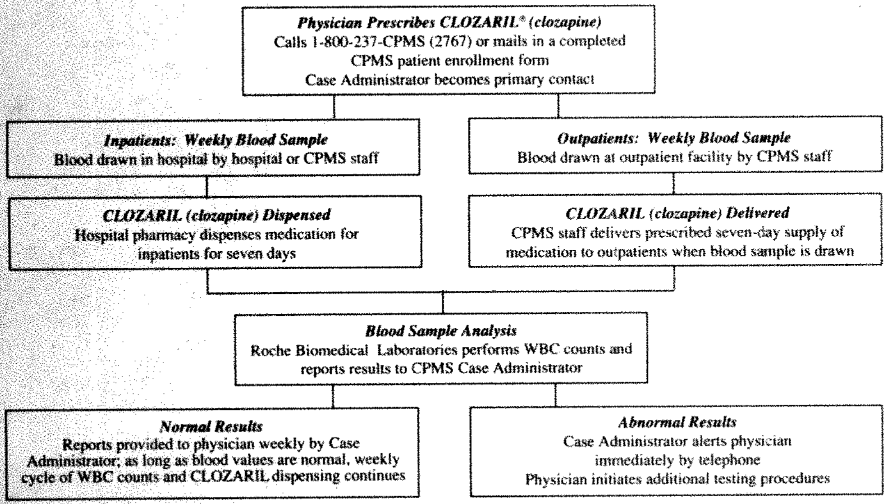
A CPMS Case Administrator coordinates WBC testing, reporting and drug delivery. For inpatients, weekly monitoring is performed in the hospital. Case Administrators arrange for weekly monitoring of outpatients. If a WBC test is missed, the Case Administrator will reschedule collection and pickup to transport the blood specimen to the laboratory.

When the patient's blood sample is collected, a week's supply of CLOZARIL (clozapine) is dispensed (see chart). Each week, results of the WBC count are sent to the prescribing psychiatrist. The Case Administrator will alert the psychiatrist immediately by telephone if the white blood cell count drops significantly.

In addition to its safety benefits, CPMS can also enhance clinical care, according to Richard Wagner, MD. Dr. Wagner is director of the Rhode Island Psychiatric Research and Training Center, one of 16 sites selected for the U.S. multicenter CLOZARIL comparative study. He said that the weekly patient follow-up provided by CPMS often improves compliance with the drug regimen and decreases recidivism. Some patients chronically hospitalized will respond so dramatically they can be discharged.

Clinicians who would like more information about CPMS may contact their Sandoz Mental Health Sales Representative. ■

### How the Clozaril Patient Management System$^{SM}$ (CPMS$^{SM}$) Works


*Physician Prescribes CLOZARIL® (clozapine)*
Calls 1-800-237-CPMS (2767) or mails in a completed CPMS patient enrollment form
Case Administrator becomes primary contact
*Inpatients: Weekly Blood Sample*
Blood drawn in hospital by hospital or CPMS staff
*Outpatients: Weekly Blood Sample*
Blood drawn at outpatient facility by CPMS staff
*CLOZARIL (clozapine) Dispensed*
Hospital pharmacy dispenses medication for inpatients for seven days
*CLOZARIL (clozapine) Delivered*
CPMS staff delivers prescribed seven-day supply of medication to outpatients when blood sample is drawn
*Blood Sample Analysis*
Roche Biomedical Laboratories performs WBC counts and reports results to CPMS Case Administrator
*Normal Results*
Reports provided to physician weekly by Case Administrator; as long as blood values are normal, weekly cycle of WBC counts and CLOZARIL dispensing continues
*Abnormal Results*
Case Administrator alerts physician immediately by telephone
Physician initiates additional testing procedures

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# Side Effects Profile

*(Continued from page 3)*

study, the mean and median doses were both approximately 600 mg/day. Patients must be advised not to engage in any activity where sudden loss of consciousness could cause serious risk to themselves or others, e.g., the operation of complex machinery, driving an automobile, swimming, climbing, etc.

Particular attention should be paid to patients with underlying cardiovascular disease or arrhythmias. Sustained tachycardia is a frequent occurrence in patients (25%) taking CLOZARIL tablets, with patients having an average increase in pulse rate of 10-15 bpm. Hypotension (9%) and hypertension (4%) are other cardiovascular effects associated with CLOZARIL (clozapine). ■

# Management System Frees Psychiatrists From Routine Tasks

The Clozaril Patient Management System$^{SM}$ (CPMS$^{SM}$) relieves psychiatrists of the burden of hematological monitoring that must accompany CLOZARIL® therapy. The mandatory weekly white blood cell counts are conducted by Caremark Homecare, Inc., a national home healthcare agency, under the supervision of an agency Case Administrator, who arranges for the specimens to be transported and analyzed by Roche Biomedical Laboratories, a national clinical laboratory.

The physician need only call 1-800-237-CPMS (2767) to prescribe CLOZARIL (clozapine) or mail in a completed CPMS patient enrollment form. Thereafter, the Case Administrator will coordinate blood testing and drug dispensing, and report blood test results to the prescribing psychiatrist. At all times, the physician retains clinical control of the patient.

When the patient's WBC count is normal, the drug will be dispensed routinely, with the report mailed to the psychiatrist. Should a drop in WBC count occur, the psychiatrist will be contacted immediately by telephone. ■

# Investigators Report Virtual Absence of Certain Acute EPS

Unlike standard antipsychotics, a virtual absence of certain acute extrapyramidal side effects (EPS), such as acute dystonia, is associated with CLOZARIL® administration. The incidence of other EPS, such as akathisia and rigidity, is also much lower with CLOZARIL therapy than with other agents. In a double-blind comparison of CLOZARIL (clozapine) and chlorpromazine/benztropine, 11 of 76 chlorpromazine-treated patients discontinued therapy because of poorly tolerated EPS. In contrast, only one of 75 CLOZARIL patients stopped treatment because of EPS. There have been no confirmed cases of tardive dyskinesia in over 15 years' worldwide experience with clozapine. ■

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**Please see brief summary of prescribing information on following page.**

# CLOZARIL®

(clozapine)
TABLETS

**CAUTION: Federal law prohibits dispensing without a prescription.**

## CONTRAINDICATIONS

CLOZARIL is contraindicated in patients with myeloproliferative disorders, or a history of CLOZARIL-induced agranulocytosis or severe granulocytopenia. CLOZARIL should not be used simultaneously with other agents having a well-known potential to suppress bone marrow function. As with more typical antipsychotic drugs, CLOZARIL is contraindicated in severe central nervous system depression or comatose states from any cause.

## WARNINGS

### General

**BECAUSE OF THE SIGNIFICANT RISK OF AGRANULOCYTOSIS, A POTENTIALLY LIFE-THREATENING ADVERSE EVENT (SEE BELOW), CLOZARIL SHOULD BE RESERVED FOR USE IN THE TREATMENT OF SEVERELY ILL SCHIZOPHRENIC PATIENTS WHO FAIL TO SHOW AN ACCEPTABLE RESPONSE TO ADEQUATE COURSES OF STANDARD ANTIPSYCHOTIC DRUG TREATMENT, EITHER BECAUSE OF INSUFFICIENT EFFECTIVENESS OR THE INABILITY TO ACHIEVE AN EFFECTIVE DOSE DUE TO INTOLERABLE ADVERSE EFFECTS FROM THOSE DRUGS. CONSEQUENTLY, BEFORE INITIATING TREATMENT WITH CLOZARIL, IT IS STRONGLY RECOMMENDED THAT A PATIENT BE GIVEN AT LEAST TWO TRIALS, EACH WITH A DIFFERENT STANDARD ANTIPSYCHOTIC DRUG PRODUCT, AT AN ADEQUATE DOSE AND FOR AN ADEQUATE DURATION.**

**PATIENTS WHO ARE BEING TREATED WITH CLOZARIL MUST HAVE A BASELINE WHITE BLOOD CELL (WBC) AND DIFFERENTIAL COUNT BEFORE INITIATION OF TREATMENT, AND A WBC COUNT EVERY WEEK THROUGHOUT TREATMENT, AND FOR FOUR WEEKS AFTER THE DISCONTINUATION OF CLOZARIL.**

**CLOZARIL IS AVAILABLE ONLY THROUGH THE CLOZARIL PATIENT MANAGEMENT SYSTEM$^{SM}$ (CPMS$^{SM}$).**

### Agranulocytosis

**Agranulocytosis, defined as a granulocyte count (polys + bands) of less than 500 per $mm^3$, has been estimated to occur in association with CLOZARIL use at a cumulative incidence at one year of approximately 1.3%, based on the occurrence of 15 U.S. cases out of 1743 patients exposed to CLOZARIL during its clinical testing prior to domestic marketing. All of these cases occurred at a time when the need for close monitoring of WBC counts was already recognized. This reaction could prove fatal if not detected early and therapy interrupted. While no fatalities have been associated with the U.S. agranulocytosis cases, and all cases have recovered fully, the U.S. sample is too small to reliably estimate the case fatality rate. Of the 112 cases of agranulocytosis reported worldwide in association with CLOZARIL use as of December 31, 1986, 35% were fatal. However, few of these deaths occurred since 1977, at which time the knowledge of CLOZARIL-induced agranulocytosis became more widespread, and close monitoring of WBC counts more widely practiced. Nevertheless, it is unknown at present what the case fatality rate will be for CLOZARIL-induced agranulocytosis, despite strict adherence to the recommendation for weekly monitoring of WBC counts.**

**Treatment should not be initiated if the WBC count is less than 3500 per $mm^3$, or if the patient has a history of a myeloproliferative disorder, or previous CLOZARIL-induced agranulocytosis or granulocytopenia. Patients should be advised to report immediately the appearance of lethargy, weakness, fever, sore throat or any other signs of infection. If, after the initiation of treatment, the total WBC count has dropped below 3500 per $mm^3$ or it has dropped by a substantial amount from baseline, even if the count is above 3500 per $mm^3$, or if immature forms are present, a repeat WBC count and a differential count should be done. If subsequent WBC counts and the differential count reveal a total WBC count between 3000 and 3500 per $mm^3$ and a granulocyte count above 1500 per $mm^3$, twice weekly WBC counts and differential counts should be performed.**

**If the total WBC count falls below 3000 per $mm^3$ or the granulocyte count below 1500 per $mm^3$, CLOZARIL therapy should be interrupted and patients should be carefully monitored for flu-like symptoms or other symptoms suggestive of infection. CLOZARIL therapy may be resumed if no symptoms of infection develop, and if the total WBC count returns to levels above 3000 per $mm^3$ and the granulocyte count returns to levels above 1500 per $mm^3$. However, in this event, twice-weekly WBC counts and differential counts should continue until total WBC counts return to levels above 3500 per $mm^3$.**

**If the total WBC count falls below 2000 per $mm^3$ or the granulocyte count falls below 1000 per $mm^3$, bone marrow aspiration should be considered to ascertain granulopoietic status. Protective isolation with close observation may be indicated if granulopoiesis is determined to be deficient. Should evidence of infection develop, the patient should have appropriate cultures performed and an appropriate antibiotic regimen instituted.**

**Patients whose total WBC counts fall below 2000 per $mm^3$, or granulocyte counts below 1000 per $mm^3$ during CLOZARIL therapy should *not* be re-challenged with CLOZARIL. Patients discontinued from CLOZARIL therapy due to significant WBC suppression have been found to develop agranulocytosis upon re-challenge, often with a shorter latency on re-exposure. To reduce the chances of re-challenge occurring in patients who have experienced significant bone marrow suppression during CLOZARIL therapy, a single, national master file will be maintained confidentially within the CPMS (Clozaril Patient Management System).**

**Except for evidence of significant bone marrow suppression during initial CLOZARIL therapy, there are no established risk factors, based on worldwide experience, for the development of agranulocytosis in association with CLOZARIL use. However, a disproportionate number of the U.S. cases of agranulocytosis occurred in patients of Jewish background compared to the overall proportion of such patients exposed during the domestic development of CLOZARIL. Most of the U.S. cases occurred within 4-10 weeks of exposure, but neither dose nor duration is a reliable predictor of this problem. No patient characteristics have been clearly linked to the development of agranulocytosis in association with CLOZARIL use, but agranulocytosis associated with other antipsychotic drugs has been reported to occur with a greater frequency in women, the elderly and in patients who are cachectic or have serious underlying medical illness; such patients may also be at particular risk with CLOZARIL.**

**To reduce the risk of agranulocytosis developing undetected, CLOZARIL will be dispensed only within the Clozaril Patient Management System.**

### Seizures

**Seizure has been estimated to occur in association with CLOZARIL use at a cumulative incidence at one year of approximately 5%, based on the occurrence of one or more seizures in 61 of 1743 patients exposed to CLOZARIL during its clinical testing prior to domestic marketing (i.e., a crude rate of 3.5%). Dose appears to be an important predictor of seizure, with a greater likelihood of seizure at the higher CLOZARIL doses used.**

**Caution should be used in administering CLOZARIL to patients having a history of seizures or other predisposing factors. Because of the substantial risk of seizure associated with CLOZARIL use, patients should be advised not to engage in any activity where sudden loss of consciousness could cause serious risk to themselves or others, e.g., the operation of complex machinery, driving an automobile, swimming, climbing, etc.**

### Adverse Cardiovascular Effects

Orthostatic hypotension can occur with CLOZARIL treatment, especially during initial titration in association with rapid dose escalation, and may represent a continuing risk in some patients. Tachycardia, which may be sustained, has also been observed in approximately 25% of patients taking CLOZARIL, with patients having an average increase in pulse rate of 10-15 bpm. The sustained tachycardia is not simply a reflex response to hypotension, and is present in all positions monitored. Either tachycardia or hypotension may pose a serious risk for an individual with compromised cardiovascular function. A minority of CLOZARIL-treated patients experience ECG repolarization changes similar to those seen with other antipsychotic drugs, including S-T segment depression and flattening or inversion of T waves, which all normalize after discontinuation of CLOZARIL. The clinical significance of these changes is unclear. However, in clinical trials with CLOZARIL, several patients experienced significant cardiac events, including ischemic changes, myocardial infarction, nonfatal arrhythmias and sudden unexplained death. Causality assessment was difficult in many of these cases because of serious preexisting cardiac disease and plausible alternative causes. Rare instances of sudden, unexplained death have been reported in psychiatric patients, with or without associated antipsychotic drug treatment, and the relationship of these events to antipsychotic drug use is unknown. CLOZARIL should be used with caution in patients with known cardiovascular disease, and the recommendation for gradual titration of dose should be carefully observed.

### Neuroleptic Malignant Syndrome

A potentially fatal symptom complex sometimes referred to as Neuroleptic Malignant Syndrome (NMS) has been reported in association with antipsychotic drugs. Clinical manifestations of NMS are hyperpyrexia, muscle rigidity, altered mental status and evidence of autonomic instability (irregular pulse or blood pressure, tachycardia, diaphoresis, and cardiac dysrhythmias). No cases of NMS have been attributed to CLOZARIL alone. However, there have been several reported cases of NMS in patients treated concomitantly with lithium or other CNS-active agents.

### Tardive Dyskinesia

A syndrome consisting of potentially irreversible, involuntary, dyskinetic movements may develop in patients treated with antipsychotic drugs. Although the prevalence of the syndrome appears to be highest among the elderly, especially elderly women, it is impossible to rely upon prevalence estimates to predict, at the inception of treatment, which patients are likely to develop the syndrome.

There are several reasons for predicting that CLOZARIL may be different from other antipsychotic drugs in its potential for inducing tardive dyskinesia, including the preclinical finding that it has a relatively weak dopamine blocking effect and the clinical finding of a virtual absence of certain acute extrapyramidal symptoms, e.g., dystonia. In addition, there have been no confirmed cases of tardive dyskinesia developing in association with CLOZARIL use. Nevertheless, it cannot yet be concluded, without more extended experience, that CLOZARIL is incapable of inducing this syndrome.

## PRECAUTIONS

Because of the significant risk of agranulocytosis and seizure, both of which present a continuing risk over time, the extended treatment of patients failing to show an acceptable level of clinical response should ordinarily be avoided. In addition, the need for continuing treatment in patients exhibiting beneficial clinical responses should be periodically re-evaluated. During CLOZARIL therapy, patients may experience transient temperature elevations above 100.4°F (38°C), with the peak incidence within the first three weeks of treatment. While this fever is generally benign and self-limiting, it may necessitate discontinuing patients from treatment. On occasion, there may be an associated increase or decrease in WBC count. Patients with fever should be carefully evaluated to rule out the possibility of an underlying infectious process or the development of agranulocytosis. In the presence of high fever, the possibility of neuroleptic malignant syndrome (NMS) must be considered. CLOZARIL has very potent anticholinergic effects, and great care should be exercised in using this drug in the presence of prostatic enlargement or narrow angle glaucoma. Because of initial sedation, CLOZARIL may impair mental and/or physical abilities, especially during the first few days of therapy. The recommendations for gradual dose escalation should be carefully adhered to, and patients cautioned about activities requiring alertness. Clinical experience with CLOZARIL in patients with concomitant systemic diseases is limited. Nevertheless, caution is advisable in using CLOZARIL in patients with hepatic, renal or cardiac disease.

### Information for Patients

Patients who are to receive CLOZARIL should be warned about the significant risk of developing agranulocytosis. They should be informed that weekly blood tests are required to monitor for the occurrence of agranulocytosis, and that CLOZARIL tablets will be made available only through a special program designed to ensure the required blood monitoring. Patients should be advised to report immediately the appearance of lethargy, weakness, fever, sore throat, malaise, mucous membrane ulceration or other possible signs of infection. Particular attention should be paid to any flu-like complaints or other symptoms that might suggest infection. Patients should be informed of the significant risk of seizure during CLOZARIL treatment, and they should be advised to avoid driving and any other potentially hazardous activity while taking CLOZARIL. Patients should be advised of the risk of orthostatic hypotension, especially during the period of initial dose titration. Patients should notify their physician if they are taking, or plan to take, any prescription or over-the-counter drugs or alcohol. Patients should notify their physician if they become pregnant or intend to become pregnant during therapy. Patients should not breast feed an infant if they are taking CLOZARIL.

# CLOZARIL®

(clozapine)

TABLETS

**Drug Interactions**

The risks of using CLOZARIL in combination with other drugs have not been systematically evaluated. The mechanism of CLOZARIL-induced agranulocytosis is unknown; nonetheless, the possibility that causative factors may interact synergistically to increase the risk and/or severity of bone marrow suppression warrants consideration. Therefore, CLOZARIL should not be used with other agents having a well-known potential to suppress bone marrow function. Given the primary CNS effects of CLOZARIL, caution is advised in using it concomitantly with other CNS-active drugs. Because CLOZARIL is highly bound to serum protein, the administration of CLOZARIL to a patient taking another drug which is highly bound to protein (e.g., warfarin, digoxin) may cause an increase in plasma concentrations of these drugs, potentially resulting in adverse effects. Conversely, adverse effects may result from displacement of protein-bound CLOZARIL by other highly bound drugs.

**CLOZARIL may also potentiate the hypotensive effects of antihypertensive drugs and the anticholinergic effects of atropine-type drugs. The administration of epinephrine should be avoided in the treatment of drug-induced hypotension because of a possible reverse epinephrine effect.**

**Pregnancy Category B**

There are no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, and in view of the desirability of keeping the administration of all drugs to a minimum during pregnancy, this drug should be used only if clearly needed.

**ADVERSE REACTIONS**

Adverse events observed in association with the use of CLOZARIL in clinical trials at an incidence of 5% or greater were: central nervous system complaints, including drowsiness/sedation, dizziness/vertigo, headache and tremor; autonomic nervous system complaints, including salivation, sweating, dry mouth and visual disturbances; cardiovascular findings, including tachycardia, hypotension and syncope; and gastrointestinal complaints, including constipation and nausea; and fever. Complaints of drowsiness/sedation tend to subside with continued therapy or dose reduction. Salivation may be profuse, especially during sleep, but may be diminished with dose reduction.

**DOSAGE AND ADMINISTRATION**

**Initial Treatment**

It is recommended that treatment with CLOZARIL begin at 25 mg once or twice daily, and then be continued with daily dosage increments of 25 to 50 mg/day, if well-tolerated, to achieve a target dose of 300 to 450 mg/day by the end of two weeks. Subsequent dosage increments should be made no more than once- or twice-weekly, in increments not to exceed 100 mg. Cautious titration and a divided dosage schedule are necessary to minimize the risks of hypotension, seizure, and sedation.

**Therapeutic Dose Adjustment**

Daily dosing should continue on a divided basis as an effective and tolerable dose level is sought. While many patients may respond adequately at doses between 300-600 mg/day, it may be necessary to raise the dose to the 600-900 mg/day range to obtain an acceptable response. [Note: In the multicenter study providing the primary support for the superiority of CLOZARIL in treatment resistant patients, the mean and median CLOZARIL doses were both approximately 600 mg/day.]

Because of the possibility of increased adverse reactions at higher doses, particularly seizures, patients should ordinarily be given adequate time to respond to a given dose level before escalation to a higher dose is contemplated.

Dosing should not exceed 900 mg/day.

**Discontinuation of Treatment**

In the event of planned termination of CLOZARIL therapy, gradual reduction in dose is recommended over a 1 to 2 week period. However, should a patient's medical condition require abrupt discontinuation (e.g., leukopenia), the patient should be carefully observed for the recurrence of psychotic symptoms.

**CLOZARIL is available only through the Clozaril Patient Management System, a program that combines white blood cell testing, patient monitoring, pharmacy, and drug distribution services, all linked to compliance with required safety monitoring.**

**To prescribe CLOZARIL call 1-800-237-CPMS (2767) or mail in a completed CPMS Enrollment Form.**

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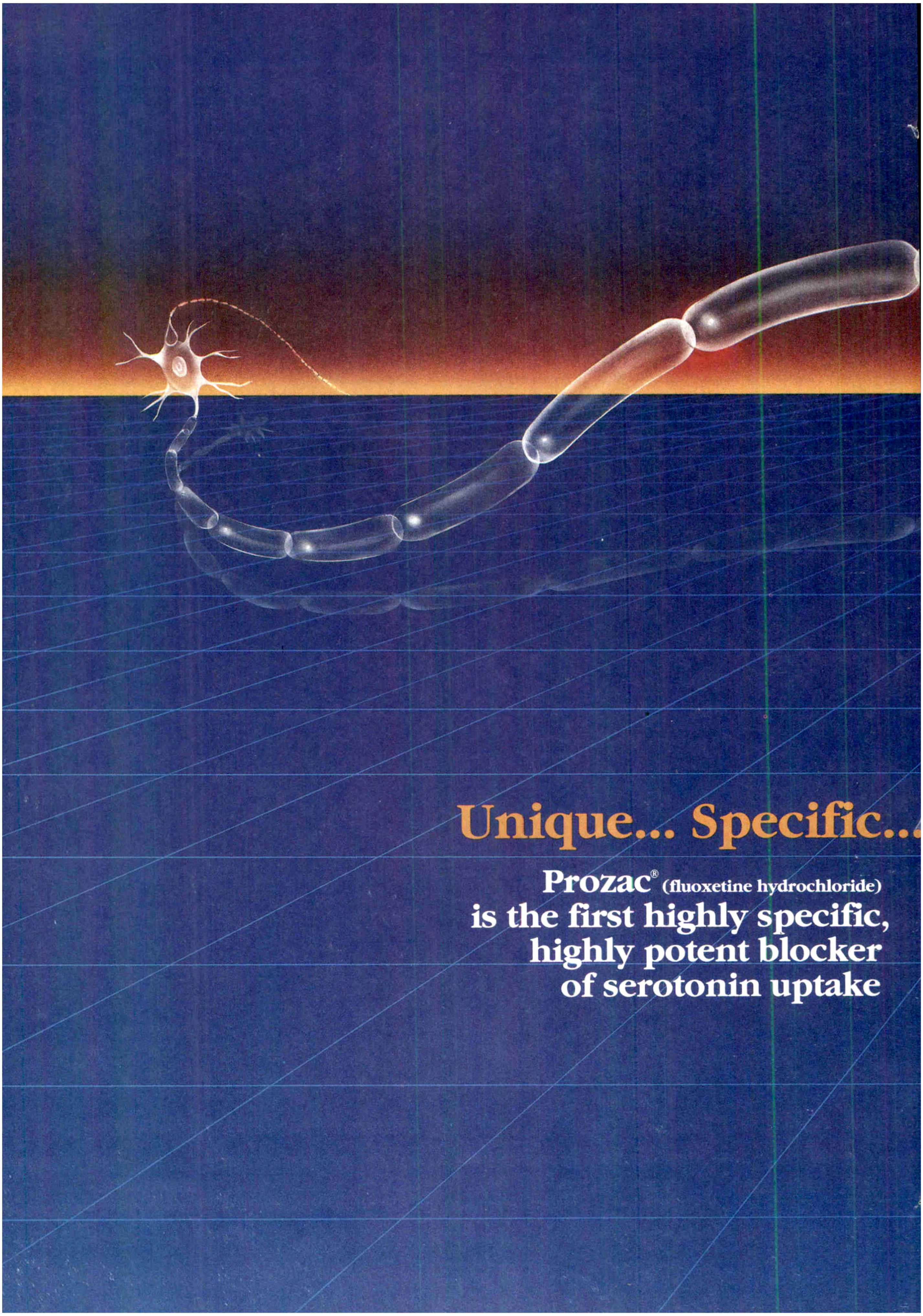

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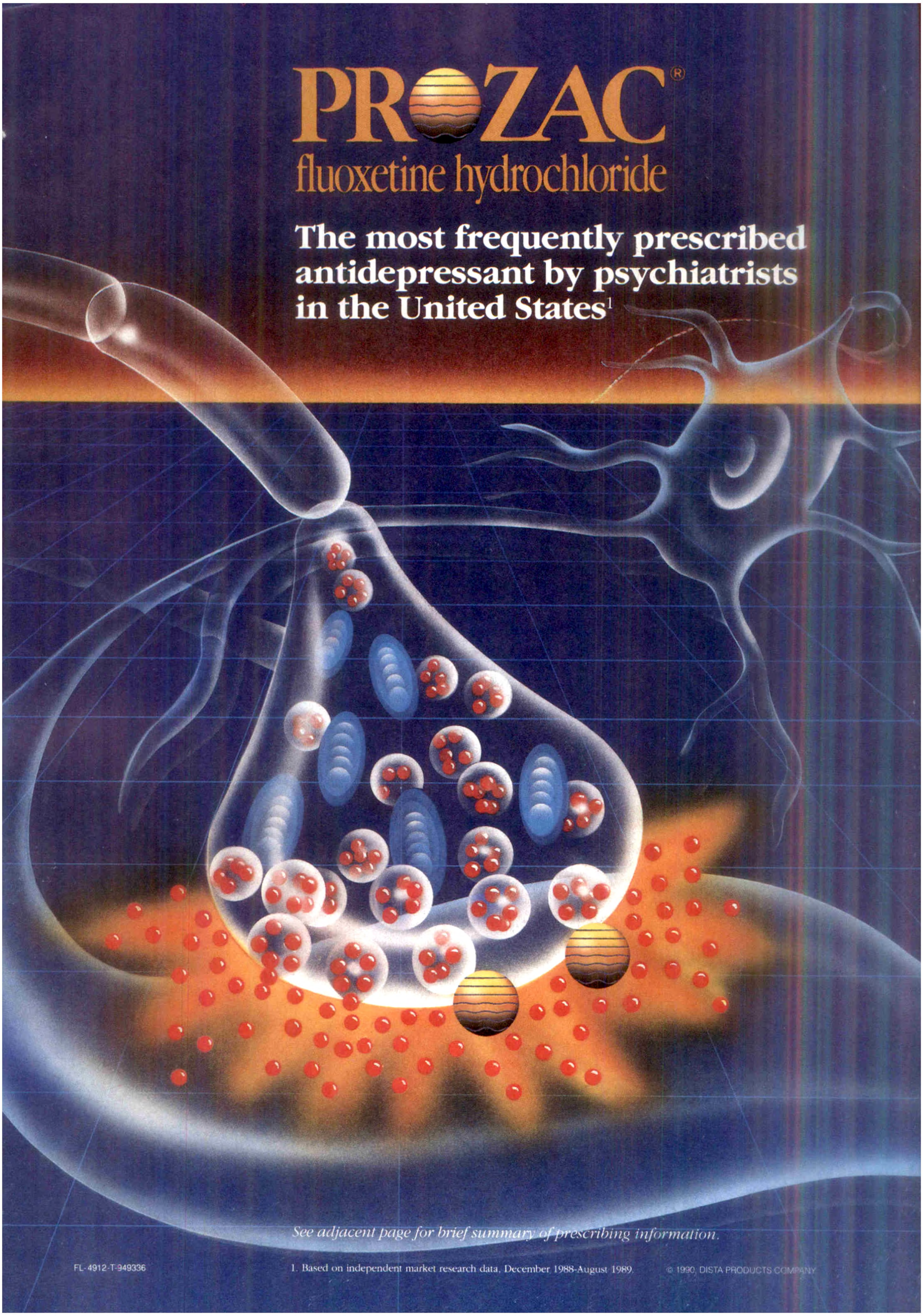
of serotonin uptake



PROZAC®
fluoxetine hydrochloride

**The most frequently prescribed antidepressant by psychiatrists in the United States**[1]

*See adjacent page for brief summary of prescribing information.*

FL-4912-T-949336

[1] Based on independent market research data, December 1988-August 1989.

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# **Prozac**®(fluoxetine hydrochloride)

**Brief Summary:**
**Consult the package literature for complete information.**

**Indications:** Prozac is indicated for the treatment of depression.

**Contraindication:** Prozac is contraindicated in patients known to be hypersensitive to it.

**Warnings:** *Monoamine Oxidase Inhibitors* — Data on the effects of the combined use of fluoxetine and MAO inhibitors are limited. Their combined use should be avoided. Based on experience with the combined administration of MAOIs and tricyclics, at least 14 days should elapse between discontinuation of an MAO inhibitor and initiation of treatment with fluoxetine.

Because of the long half-lives of fluoxetine and its active metabolite, at least five weeks (approximately five half-lives of norfluoxetine) should elapse between discontinuation of fluoxetine and initiation of therapy with an MAOI. Administration of an MAOI within five weeks of discontinuation of fluoxetine may increase the risk of serious events. While a causal relationship to fluoxetine has not been established, death has been reported to occur following the initiation of MAOI therapy shortly after discontinuation of fluoxetine.

*Rash and Accompanying Events* — During premarketing testing of more than 5,600 US patients given fluoxetine, approximately 4% developed a rash and/or urticaria. Among these cases, almost a third were withdrawn from treatment because of the rash and/or systemic signs or symptoms associated with the rash. Clinical findings reported in association with rash include fever, leukocytosis, arthralgias, edema, carpal tunnel syndrome, respiratory distress, lymphadenopathy, proteinuria, and mild transaminase elevation. Most patients improved promptly with discontinuation of fluoxetine and/or adjunctive treatment with antihistamines or steroids, and all patients experiencing these events were reported to recover completely.

Two patients are known to have developed a serious cutaneous systemic illness. In neither patient was there an unequivocal diagnosis, but one was considered to have a leukocytoclastic vasculitis, and the other, a severe desquamating syndrome that was considered variously to be a vasculitis or erythema multiforme. Several other patients have had systemic syndromes suggestive of serum sickness.

Since the introduction of Prozac, systemic events, possibly related to vasculitis, have developed in patients with rash. Although these events are rare, they may be serious, involving the lung, kidney, or liver. Death has been reported to occur in association with these systemic events.

Whether these systemic events and rash have a common underlying cause or are due to different etiologies or pathogenic processes is not known. Upon the appearance of rash, Prozac should be discontinued.

**Precautions:** *General* — Anxiety and Insomnia — Anxiety, nervousness, and insomnia were reported by 10% to 15% of patients treated with Prozac. These symptoms led to drug discontinuation in 5% of patients treated with Prozac.

Altered Appetite and Weight — Significant weight loss, especially in underweight depressed patients, may be an undesirable result of treatment with Prozac.

In controlled clinical trials, approximately 9% of patients treated with Prozac experienced anorexia. This incidence is approximately sixfold that seen in placebo controls. A weight loss of greater than 5% of body weight occurred in 13% of patients treated with Prozac compared to 4% of placebo- and 3% of tricyclic-antidepressant-treated patients. However, only rarely have patients been discontinued from treatment with Prozac because of weight loss.

Activation of Mania/Hypomania — During premarketing testing, hypomania or mania occurred in approximately 1% of fluoxetine-treated patients. Activation of mania/hypomania has also been reported in a small proportion of patients with Major Affective Disorder treated with other marketed antidepressants.

Seizures — Twelve patients among more than 6,000 evaluated worldwide in the course of premarketing development of fluoxetine experienced convulsions (or events described as possibly having been seizures), a rate of 0.2% that appears to be similar to that associated with other marketed antidepressants. Prozac should be introduced with care in patients with a history of seizures.

Suicide — The possibility of a suicide attempt is inherent in depression and may persist until significant remission occurs. Close supervision of high-risk patients should accompany initial drug therapy. Prescriptions for Prozac should be written for the smallest quantity of capsules consistent with good patient management, in order to reduce the risk of overdose.

The Long Elimination Half-Lives of Fluoxetine and Its Metabolites — Because of the long elimination half-lives of the parent drug (two to three days) and its major active metabolite (seven to nine days), changes in dose will not be fully reflected in plasma for several weeks, affecting both strategies for titration to final dose and withdrawal from treatment (*see* Clinical Pharmacology *and* Dosage and Administration).

Use in Patients With Concomitant Illness — Clinical experience with Prozac in patients with concomitant systemic illness is limited. Caution is advisable in using Prozac in patients with diseases or conditions that could affect metabolism or hemodynamic responses.

Fluoxetine has **not** been evaluated or used to any appreciable extent in patients with a recent history of myocardial infarction or unstable heart disease. Patients with these diagnoses were systematically excluded from clinical studies during the product's premarket testing. However, the electrocardiograms of 312 patients who received Prozac in double-blind trials were retrospectively evaluated; no conduction abnormalities that resulted in heart block were observed. The mean heart rate was reduced by approximately three beats/min.

In subjects with cirrhosis of the liver, the clearances of fluoxetine and its active metabolite, norfluoxetine, were decreased, thus increasing the elimination half-lives of these substances. A lower or less frequent dose should be used in patients with cirrhosis.

Since fluoxetine is extensively metabolized, excretion of unchanged drug in urine is a minor route of elimination. However, until adequate numbers of patients with severe renal impairment have been evaluated during chronic treatment with fluoxetine, it should be used with caution in such patients.

In patients with diabetes, Prozac may alter glycemic control. Hypoglycemia has occurred during therapy with Prozac, and hyperglycemia has developed following discontinuation of the drug. As is true with many other types of medication when taken concurrently by patients with diabetes, insulin and/or oral hypoglycemic dosage may need to be adjusted when therapy with Prozac is instituted or discontinued.

Interference With Cognitive and Motor Performance — Any psychoactive drug may impair judgment, thinking, or motor skills, and patients should be cautioned about operating hazardous machinery, including automobiles, until they are reasonably certain that the drug treatment does not affect them adversely.

*Information for Patients* — Physicians are advised to discuss the following issues with patients for whom they prescribe Prozac:

Because Prozac may impair judgment, thinking, or motor skills, patients should be advised to avoid driving a car or operating hazardous machinery until they are reasonably certain that their performance is not affected.

Patients should be advised to inform their physician if they are taking or plan to take any prescription or over-the-counter drugs or alcohol.

Patients should be advised to notify their physician if they become pregnant or intend to become pregnant during therapy.

Patients should be advised to notify their physician if they are breast feeding an infant.

Patients shoud be advised to notify their physician if they develop a rash or hives.

*Laboratory Tests* — There are no specific laboratory tests recommended.

*Drug Interactions* — As with all drugs, the potential for interaction by a variety of mechanisms (ie, pharmacodynamic, pharmacokinetic drug inhibition or enhancement, etc) is a possibility (*see* Accumulation and Slow Elimination *under* Clinical Pharmacology).

Tryptophan — Five patients receiving Prozac in combination with tryptophan experienced adverse reactions, including agitation, restlessness, and gastrointestinal distress.

Monoamine Oxidase Inhibitors — *See* Warnings.

Other Antidepressants — There have been greater than twofold increases of previously stable plasma levels of other antidepressants when Prozac has been administered in combination with these agents (*see* Accumulation and Slow Elimination *under* Clinical Pharmacology).

Lithium — There have been reports of both increased and decreased lithium levels when lithium was used concomitantly with fluoxetine. Cases of lithium toxicity have been reported. Lithium levels should be monitored when these drugs are administered concomitantly.

Diazepam Clearance — The half-life of concurrently administered diazepam may be prolonged in some patients (*see* Accumulation and Slow Elimination *under* Clinical Pharmacology).

Potential Effects of Coadministration of Drugs Highly Bound to Plasma Proteins — Because fluoxetine is tightly bound to plasma protein, the administration of fluoxetine to a patient taking another drug that is tightly bound to protein (eg, Coumadin, digitoxin) may cause a shift in plasma concentrations potentially resulting in an adverse effect. Conversely, adverse effects may result from displacement of protein-bound fluoxetine by other tightly bound drugs (*see* Accumulation and Slow Elimination *under* Clinical Pharmacology).

CNS-Active Drugs — The risk of using Prozac in combination with other CNS-active drugs has not been systematically evaluated. Consequently, caution is advised if the concomitant administration of Prozac and such drugs is required (*see* Accumulation and Slow Elimination *under* Clinical Pharmacology).

Electroconvulsive Therapy — There are no clinical studies establishing the benefit of the combined use of ECT and fluoxetine. A single report of a prolonged seizure in a patient on fluoxetine has been reported.

*Carcinogenesis, Mutagenesis, Impairment of Fertility* — There is no evidence of carcinogenicity, mutagenicity, or impairment of fertility with Prozac.

The dietary administration of fluoxetine to rats and mice for two years at levels equivalent to approximately 7.5 and 9.0 times the maximum human dose (80 mg) respectively produced no evidence of carcinogenicity.

Fluoxetine and norfluoxetine have been shown to have no genotoxic effects based on the following assays: bacterial mutation assay, DNA repair assay in cultured rat hepatocytes, mouse lymphoma assay, and in vivo sister chromatid exchange assay in Chinese hamster bone marrow cells.

Two fertility studies conducted in rats at doses of approximately five and nine times the maximum human dose (80 mg) indicated that fluoxetine had no adverse effects on fertility. A slight decrease in neonatal survival was noted, but this was probably associated with depressed maternal food consumption and suppressed weight gain.

*Pregnancy* — Teratogenic Effects — Pregnancy Category B — Reproduction studies have been performed in rats and rabbits at doses nine and 11 times the maximum daily human dose (80 mg) respectively and have revealed no evidence of harm to the fetus due to Prozac. There are, however, no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

*Labor and Delivery* — The effect of Prozac on labor and delivery in humans is unknown.

*Nursing Mothers* — Because many drugs are excreted in human milk, caution should be exercised when Prozac is administered to a nursing woman. In one breast milk sample, the concentration of fluoxetine plus norfluoxetine was 70.4 ng/mL. The concentration in the mother's plasma was 295.0 ng/mL. No adverse effects on the infant were reported.

*Usage in Children* — Safety and effectiveness in children have not been established.

*Usage in the Elderly* — Prozac has not been systematically evaluated in older patients; however, several hundred elderly patients have participated in clinical studies with Prozac, and no unusual adverse age-related phenomena have been identified. However, these data are insufficient to rule out possible age-related differences during chronic use, particularly in elderly patients who have concomitant systemic illnesses or who are receiving concomitant drugs.

*Hyponatremia* — Several cases of hyponatremia (some with serum sodium lower than 110 mmol/L) have been reported. The hyponatremia appeared to be reversible when Prozac was discontinued. Although these cases were complex with varying possible etiologies, some were possibly due to the syndrome of inappropriate antidiuretic hormone secretion (SIADH). The majority of these occurrences have been in older patients and in patients taking diuretics or who were otherwise volume depleted.

**Adverse Reactions:** *Commonly Observed* — The most commonly observed adverse events associated with the use of Prozac and not seen at an equivalent incidence among placebo-treated patients were: nervous system complaints, including anxiety, nervousness, and insomnia; drowsiness and fatigue or asthenia; tremor; sweating; gastrointestinal complaints, including anorexia, nausea, and diarrhea; and dizziness or lightheadedness.

*Associated With Discontinuation of Treatment* — Fifteen percent of approximately 4,000 patients who received Prozac in US premarketing clinical trials discontinued treatment due to an adverse event. The more common events causing discontinuation included: psychiatric (5.3%), primarily nervousness, anxiety, and insomnia; digestive (3.0%), primarily nausea; nervous system (1.6%), primarily dizziness; body as a whole (1.5%), primarily asthenia and headache; and skin (1.4%), primarily rash and pruritus.

*Incidence in Controlled Clinical Trials* — The table that follows enumerates adverse events that occurred at a frequency of 1% or more among Prozac-treated patients who participated in controlled trials comparing Prozac with placebo. The prescriber should be aware that these figures cannot be used to predict the incidence of side effects in the course of usual medical practice where patient characteristics and other factors differ from those that prevailed in the clinical trials. Similarly, the cited frequencies cannot be compared with figures obtained from other clinical investigations involving different treatments, uses, and investigators. The cited figures, however, do provide the prescribing physician with some basis for estimating the relative contribution of drug and nondrug factors to the side-effect incidence rate in the population studied.

TREATMENT-EMERGENT ADVERSE EXPERIENCE INCIDENCE
IN PLACEBO-CONTROLLED CLINICAL TRIALS

| Body System/ Adverse Event* | Percentage of Patients Reporting Event Prozac (N = 1,730) | Percentage of Patients Reporting Event Placebo (N = 799) |
|---|---|---|
| **Nervous** | | |
| Headache | 20.3 | 15.5 |
| Nervousness | 14.9 | 8.5 |
| Insomnia | 13.8 | 7.1 |
| Drowsiness | 11.6 | 6.3 |
| Anxiety | 9.4 | 5.5 |
| Tremor | 7.9 | 2.4 |
| Dizziness | 5.7 | 3.3 |
| Fatigue | 4.2 | 1.1 |
| Sedated | 1.9 | 1.3 |
| Sensation disturbance | 1.7 | 2.0 |
| Libido, decreased | 1.6 | — |
| Light-headedness | 1.6 | — |
| Concentration, decreased | 1.5 | — |
| **Digestive** | | |
| Nausea | 21.1 | 10.1 |
| Diarrhea | 12.3 | 7.0 |
| Mouth dryness | 9.5 | 6.0 |
| Anorexia | 8.7 | 1.5 |
| Dyspepsia | 6.4 | 4.3 |
| Constipation | 4.5 | 3.3 |
| Pain, abdominal | 3.4 | 2.9 |
| Vomiting | 2.4 | 1.3 |
| Taste change | 1.8 | — |
| Flatulence | 1.6 | 1.1 |
| Gastroenteritis | 1.0 | 1.4 |
| **Skin and Appendages** | | |
| Sweating, excessive | 8.4 | 3.8 |
| Rash | 2.7 | 1.8 |
| Pruritus | 2.4 | 1.4 |
| **Body as a Whole** | | |
| Asthenia | 4.4 | 1.9 |
| Infection, viral | 3.4 | 3.1 |
| Pain, limb | 1.6 | 1.1 |
| Fever | 1.4 | — |
| Pain, chest | 1.3 | 1.1 |
| Allergy | 1.2 | 1.1 |
| Influenza | 1.2 | 1.5 |
| **Respiratory** | | |
| Upper respiratory infection | 7.6 | 6.0 |
| Flu-like syndrome | 2.8 | 1.9 |
| Pharyngitis | 2.7 | 1.3 |
| Nasal congestion | 2.6 | 2.3 |
| Headache, sinus | 2.3 | 1.8 |
| Sinusitis | 2.1 | 2.0 |
| Cough | 1.6 | 1.6 |
| Dyspnea | 1.4 | — |
| **Cardiovascular** | | |
| Hot flushes | 1.8 | 1.0 |
| Palpitations | 1.3 | 1.4 |
| **Musculoskeletal** | | |
| Pain, back | 2.0 | 2.4 |
| Pain, joint | 1.2 | 1.1 |
| Pain, muscle | 1.2 | 1.0 |
| **Urogenital** | | |
| Menstruation, painful | 1.9 | 1.4 |
| Sexual dysfunction | 1.9 | — |
| Frequent micturition | 1.6 | — |
| Urinary tract infection | 1.2 | — |
| **Special Senses** | | |
| Vision disturbance | 2.8 | 1.8 |

*Events reported by at least 1% of Prozac-treated patients are included.
— Incidence less than 1%.

*Other Events Observed During the Premarketing Evaluation of Prozac* — During clinical testing in the US, multiple doses of Prozac were administered to approximately 5,600 subjects. Untoward events associated with this exposure were recorded by clinical investigators using descriptive terminology of their own choosing. Consequently, it is not possible to provide a meaningful estimate of the proportion of individuals experiencing adverse events without first grouping similar types of untoward events into a limited (ie, reduced) number of standardized event categories.

In the tabulations which follow, a standard COSTART Dictionary terminology has been used to classify reported adverse events. The frequencies presented, therefore, represent the proportion of the 5,600 individuals exposed to Prozac who experienced an event of the type cited on at least one occasion while receiving Prozac. All reported events are included except those already listed in tables, those COSTART terms so general as to be uninformative, and those events where a drug cause was remote. It is important to emphasize that, although the events reported did occur during treatment with Prozac, they were not necessarily caused by it.

Events are further classified within body system categories and enumerated in order of decreasing frequency using the following definitions frequent adverse events are defined as those occuring on one or more occasions in at least 1/100 patients; infrequent adverse events are those occurring in 1/100 to 1/1,000 patients; rare events are those occurring in less than 1/1,000 patients.

Body as a Whole — *Frequent:* chills; *Infrequent:* chills and fever, cyst, face edema, hangover effect, jaw pain, malaise, neck pain, neck rigidity, and pelvic pain; *Rare:* abdomen enlarged, cellulitis, hydrocephalus, hypothermia, LE syndrome, moniliasis, and serum sickness.

Cardiovascular System — *Infrequent:* angina pectoris, arrhythmia, hemorrhage, hypertension, hypotension, migraine, postural hypotension, syncope, and tachycardia; *Rare:* AV block first-degree, bradycardia, bundle-branch block, cerebral ischemia, myocardial infarct, thrombophlebitis, vascular headache, and ventricular arrhythmia.

Digestive System — *Frequent:* increased appetite; *Infrequent:* aphthous stomatitis, dysphagia, eructation, esophagitis, gastritis, gingivitis, glossitis, liver function tests abnormal, melena, stomatitis, thirst; *Rare:* bloody diarrhea, cholecystitis, cholelithiasis, colitis, duodenal ulcer, enteritis, fecal incontinence, hematemesis, hepatitis, hepatomegaly, hyperchlorhydria, increased salivation, jaundice, liver tenderness, mouth ulceration, salivary gland enlargement, stomach ulcer, tongue discoloration, and tongue edema.

Endocrine System — *Infrequent:* hypothyroidism; *Rare:* goiter and hyperthyroidism.

Hemic and Lymphatic System — *Infrequent:* anemia and lymphadenopathy; *Rare:* bleeding time increased, blood dyscrasia, leukopenia, lymphocytosis, petechia, purpura, sedimentation rate increased, and thrombocythemia.

Metabolic and Nutritional — *Frequent:* weight loss; *Infrequent:* generalized edema, hypoglycemia, peripheral edema, and weight gain; *Rare:* dehydration, gout, hypercholesteremia, hyperglycemia, hyperlipemia, hypoglycemic reaction, hypokalemia, hyponatremia, and iron deficiency anemia.

Musculoskeletal System — *Infrequent:* arthritis, bone pain, bursitis, tenosynovitis, and twitching; *Rare:* bone necrosis, chondrodystrophy, muscle hemorrhage, myositis, osteoporosis, pathological fracture, and rheumatoid arthritis.

Nervous System — *Frequent:* abnormal dreams and agitation; *Infrequent:* abnormal gait, acute brain syndrome, akathisia, amnesia, apathy, ataxia, buccoglossal syndrome, CNS stimulation, convulsion, delusions, depersonalization, emotional lability, euphoria, hallucinations, hostility, hyperkinesia, hypesthesia, incoordination, libido increased, manic reaction, neuralgia, neuropathy, paranoid reaction, psychosis, and vertigo; *Rare:* abnormal electroencephalogram, antisocial reaction, chronic brain syndrome, circumoral paresthesia, CNS depression, coma, dysarthria, dystonia, extrapyramidal syndrome, hypertonia, hysteria, myoclonus, nystagmus, paralysis, reflexes decreased, stupor, and torticollis.

Respiratory System — *Frequent:* bronchitis, rhinitis, and yawn; *Infrequent:* asthma, epistaxis, hiccup, hyperventilation, and pneumonia; *Rare:* apnea, hemoptysis, hypoxia, larynx edema, lung edema, lung fibrosis/alveolitis, and pleural effusion.

Skin and Appendages — *Infrequent:* acne, alopecia, contact dermatitis, dry skin, herpes simplex, maculopapular rash, and urticaria; *Rare:* eczema, erythema multiforme, fungal dermatitis, herpes zoster, hirsutism, psoriasis, purpuric rash, pustular rash, seborrhea, skin discoloration, skin hypertrophy, subcutaneous nodule, and vesiculobullous rash.

Special Senses — *Infrequent:* amblyopia, conjunctivitis, ear pain, eye pain, mydriasis, photophobia, and tinnitus; *Rare:* blepharitis, cataract, corneal lesion, deafness, diplopia, eye hemorrhage, glaucoma, iritis, ptosis, strabismus, and taste loss.

Urogenital System — *Infrequent:* abnormal ejaculation, amenorrhea, breast pain, cystitis, dysuria, fibrocystic breast, impotence, leukorrhea, menopause, menorrhagia, ovarian disorder, urinary incontinence, urinary retention, urinary urgency, urination impaired, and vaginitis; *Rare:* abortion, albuminuria, breast enlargement, dyspareunia, epididymitis, female lactation, hematuria, hypomenorrhea, kidney calculus, metrorrhagia, orchitis, polyuria, pyelonephritis, pyuria, salpingitis, urethral pain, urethritis, urinary tract disorder, urolithiasis, uterine hemorrhage, uterine spasm, and vaginal hemorrhage.

*Postintroduction Reports* — Voluntary reports of adverse events temporarily associated with Prozac that have been received since market introduction and which may have no causal relationship with the drug include the following: vaginal bleeding after drug withdrawal, hyperprolactinemia, thrombocytopenia, and confusion.

**Overdosage:** *Human Experience* — As of December 1987, there were two deaths among approximately 38 reports of acute overdose with fluoxetine, either alone or in combination with other drugs and/or alcohol. One death involved a combined overdose with approximately 1,800 mg of fluoxetine and an undetermined amount of maprotiline. Plasma concentrations of fluoxetine and maprotiline were 4.57 mg/L and 4.18 mg/L respectively. A second death involved three drugs yielding plasma concentrations as follows: fluoxetine, 1.93 mg/L; norfluoxetine, 1.10 mg/L; codeine, 1.80 mg/L; temazepam, 3.80 mg/L.

One other patient who reportedly took 3,000 mg of fluoxetine experienced two grand mal seizures that remitted spontaneously without specific anticonvulsant treatment (*see* Management). The actual amount of drug absorbed may have been less due to vomiting.

Nausea and vomiting were prominent in overdoses involving higher fluoxetine doses. Other prominent symptoms of overdose included agitation, restlessness, hypomania, and other signs of CNS excitation. Except for the two deaths noted above, all other overdose cases recovered without residua.

Since introduction, a single death attributed to overdose of fluoxetine alone has been reported.

PV 2474 DPP (090789)

*Additional information available to the profession on request.*

DISTA
**Dista Products Company**
Division of Eli Lilly and Company
Indianapolis, Indiana 46285

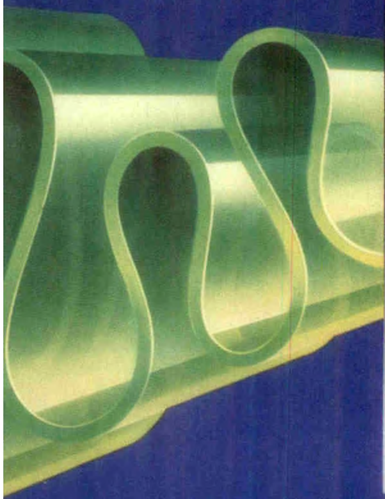
FL-4912-T-949336

Introducing
HALDOL® Decanoate 100
(HALOPERIDOL) INJECTION

Less volume per injection can enhance patient acceptance

New 100 mg/mL formulation is twice the concentration of the original 50 mg/mL decanoate formulation

- For many patients, fewer injections per dose may reduce anxiety and enhance patient compliance
- Multi-dose vial packaging means convenience for you and your staff



Please see brief summary of Prescribing Information on next page.

During dose adjustment or episodes of exacerbation of psychotic symptoms, therapy with HALDOL Decanoate 100 or HALDOL Decanoate 50 can be supplemented with short-acting forms of HALDOL® (haloperidol). The side effects of the decanoate products are those of HALDOL. The prolonged action of HALDOL Decanoate 100 and HALDOL Decanoate 50 should be considered in the management of side effects.

McNEIL
PHARMACEUTICAL
McNEILAB, INC., Spring House, PA 19477

**HALDOL® Decanoate 100**
(HALOPERIDOL) INJECTION 100mg/mL
**HALDOL® Decanoate 50**
(HALOPERIDOL) INJECTION 50mg/mL

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# HALDOL® Decanoate 100

(HALOPERIDOL) INJECTION 100mg/mL

# HALDOL® Decanoate 50

(HALOPERIDOL) INJECTION 50mg/mL

For IM Injection Only

**The following is a brief summary only. Before prescribing, see complete prescribing information in HALDOL and HALDOL Decanoate product labeling.**

**Contraindications:** Since the pharmacologic and clinical actions of HALDOL Decanoate 50 and HALDOL Decanoate 100 are attributed to HALDOL haloperidol as the active medication, Contraindications, Warnings, and additional information are those of HALDOL, modified to reflect the prolonged action.

HALDOL is contraindicated in severe toxic central nervous system depression or comatose states from any cause and in individuals who are hypersensitive to this drug or have Parkinson's disease.

**Warnings:** *Tardive Dyskinesia:* Tardive dyskinesia, a syndrome consisting of potentially irreversible, involuntary, dyskinetic movements may develop in patients treated with antipsychotic drugs. Although the prevalence of the syndrome appears to be highest among the elderly, especially elderly women, it is impossible to rely upon prevalence estimates to predict, at the inception of antipsychotic treatment, which patients are likely to develop the syndrome. Whether antipsychotic drug products differ in their potential to cause tardive dyskinesia is unknown. Both the risk of developing tardive dyskinesia and the likelihood that it will become irreversible are believed to increase as the duration of treatment and the total cumulative dose of antipsychotic drugs administered to the patient increase. However, the syndrome can develop, although much less commonly, after relatively brief treatment periods at low doses. There is no known treatment for established cases of tardive dyskinesia, although the syndrome may remit, partially or completely, if antipsychotic treatment is withdrawn. Antipsychotic treatment, itself, however, may suppress (or partially suppress) the signs and symptoms of the syndrome and thereby may possibly mask the underlying process. The effect that symptomatic suppression has upon the long-term course of the syndrome is unknown. Given these considerations, antipsychotic drugs should be prescribed in a manner that is most likely to minimize the occurrence of tardive dyskinesia. Chronic antipsychotic treatment should generally be reserved for patients who suffer from a chronic illness that 1) is known to respond to antipsychotic drugs, and 2) for whom alternative, equally effective, but potentially less harmful treatments are **not** available or appropriate. In patients who do require chronic treatment, the smallest dose and the shortest duration of treatment producing a satisfactory clinical response should be sought. The need for continued treatment should be reassessed periodically. If signs and symptoms of tardive dyskinesia appear in a patient on antipsychotics, drug discontinuation should be considered. However, some patients may require treatment despite the presence of the syndrome. (For further information about the description of tardive dyskinesia and its clinical detection, please refer to ADVERSE REACTIONS.)

*Neuroleptic Malignant Syndrome (NMS):* A potentially fatal symptom complex sometimes referred to as Neuroleptic Malignant Syndrome (NMS) has been reported in association with antipsychotic drugs. Clinical manifestations of NMS are hyperpyrexia, muscle rigidity, altered mental status (including catatonic signs) and evidence of autonomic instability (irregular pulse or blood pressure, tachycardia, diaphoresis, and cardiac dysrhythmias). Additional signs may include elevated creatine phosphokinase, myoglobinuria (rhabdomyolysis) and acute renal failure. The diagnostic evaluation of patients with this syndrome is complicated. In arriving at a diagnosis, it is important to identify cases where the clinical presentation includes both serious medical illness (e.g., pneumonia, systemic infection, etc.) and untreated or inadequately treated extrapyramidal signs and symptoms (EPS). Other important considerations in the differential diagnosis include central anticholinergic toxicity, heat stroke, drug fever and primary central nervous system (CNS) pathology. The management of NMS should include 1) immediate discontinuation of antipsychotic drugs and other drugs not essential to concurrent therapy, 2) intensive symptomatic treatment and medical monitoring, and 3) treatment of any concomitant serious medical problems for which specific treatments are available. There is no general agreement about specific pharmacological treatment regimens for uncomplicated NMS. If a patient requires antipsychotic drug treatment after recovery from NMS, the potential reintroduction of drug therapy should be carefully considered. The patient should be carefully monitored, since recurrences of NMS have been reported. Hyperpyrexia and heat stroke, not associated with the above symptom complex, have also been reported with HALDOL.

*Usage in Pregnancy:* (see PRECAUTIONS—Usage in Pregnancy) *Combined Use With Lithium:* (see PRECAUTIONS—Drug Interactions)

*General:* Bronchopneumonia, sometimes fatal, has followed use of antipsychotic drugs, including haloperidol. Prompt remedial therapy should be instituted if dehydration, hemoconcentration or reduced pulmonary ventilation occur, especially in the elderly. Decreased serum cholesterol and/or cutaneous and ocular changes have been reported with chemically-related drugs, although not with haloperidol. See PRECAUTIONS—Information for Patients for information on mental and/or physical abilities and on concomitant use with other substances.

**Precautions:** Administer cautiously to patients: (1) with severe cardiovascular disorders, due to the possibility of transient hypotension and/or precipitation of anginal pain (if a vasopressor is required, epinephrine should not be used since HALDOL may block its vasopressor activity and paradoxical further lowering of blood pressure may occur; metaraminol, phenylephrine or norepinephrine should be used); (2) receiving anticonvulsant medications, with a history of seizures, or with EEG abnormalities, because HALDOL may lower the convulsive threshold. If indicated, adequate anticonvulsant therapy should be concomitantly maintained; (3) with known allergies or a history of allergic reactions to drugs; (4) receiving anticoagulants, since an isolated instance of interference occurred with the effects of one anticoagulant (phenindione). Concomitant antiparkinson medication, if required, may have to be continued after HALDOL is discontinued because of different excretion rates; if both are discontinued simultaneously, extrapyramidal symptoms may occur. Intraocular pressure may increase when anticholinergic drugs, including antiparkinson drugs, are administered concomitantly with HALDOL. When HALDOL is used for mania in bipolar disorders, there may be a rapid mood swing to depression. Severe neurotoxicity may occur in patients with thyrotoxicosis receiving antipsychotic medication, including HALDOL.

The 1, 5, 10 mg HALDOL tablets contain FD&C Yellow No. 5 (tartrazine) which may cause allergic-type reactions (including bronchial asthma) in certain susceptible individuals, especially in those who have aspirin hypersensitivity.

*Information for Patients:* Mental and/or physical abilities required for hazardous tasks or driving may be impaired. Alcohol should be avoided due to possible additive effects and hypotension.

*Drug Interactions:* Patients receiving lithium plus haloperidol should be monitored closely for early evidence of neurological toxicity and treatment discontinued promptly if such signs appear. As with other antipsychotic agents, it should be noted that HALDOL may be capable of potentiating CNS depressants such as anesthetics, opiates, and alcohol.

*Carcinogenesis, Mutagenesis and Impairment of Fertility:* No mutagenic potential of haloperidol decanoate was found in the Ames Salmonella microsomal activation assay.

Carcinogenicity studies using oral haloperidol were conducted in Wistar rats (dosed at up to 5 mg/kg daily for 24 months) and in Albino Swiss mice (dosed at up to 5 mg/kg daily for 18 months). In the rat study survival was less than optimal in all dose groups, reducing the number of rats at risk for developing tumors. However, although a relatively greater number of rats survived to the end of the study in high dose male and female groups, these animals did not have a greater incidence of tumors than control animals. Therefore, although not optimal, this study does suggest the absence of a haloperidol related increase in the incidence of neoplasia in rats at doses up to 20 times the usual daily human dose for chronic or resistant patients. In female mice at 5 and 20 times the highest initial daily dose for chronic or resistant patients, there was a statistically significant increase in mammary gland neoplasia and total tumor incidence; at 20 times the same daily dose there was a statistically significant increase in pituitary gland neoplasia. In male mice, no statistically significant differences in incidences of total tumors or specific tumor types were noted.

Antipsychotic drugs elevate prolactin levels; the elevation persists during chronic administration. Tissue culture experiments indicate that approximately one-third of human breast cancers are prolactin dependent *in vitro*, a factor of potential importance if the prescription of these drugs is contemplated in a patient with a previously detected breast cancer. Although disturbances such as galactorrhea, amenorrhea, gynecomastia, and impotence have been reported, the clinical significance of elevated serum prolactin levels is unknown for most patients. An increase in mammary neoplasms has been found in rodents after chronic administration of antipsychotic drugs. Neither clinical studies nor epidemiologic studies conducted to date, however, have shown an association between chronic administration of these drugs and mammary tumorigenesis; the available evidence is considered too limited to be conclusive at this time.

*Usage in Pregnancy:* Pregnancy Category C. Safe use in pregnancy or in women likely to become pregnant has not been established; use only if benefit clearly justifies potential hazards to the fetus.

*Nursing Mothers:* Infants should not be nursed during drug treatment

*Pediatric Use:* Controlled trials to establish the safety and effectiveness of intramuscular administration in children have not been conducted.

**Adverse Reactions:** Adverse reactions following the administration of HALDOL Decanoate 50 or HALDOL Decanoate 100 are those of HALDOL haloperidol. Since vast experience has accumulated with HALDOL, the adverse reactions are reported for that compound as well as for haloperidol decanoate. As with all injectable medications, local tissue reactions have been reported with haloperidol decanoate

*CNS Effects: Extrapyramidal Reactions*—Neuromuscular (extrapyramidal) reactions have been reported frequently, often during the first few days of treatment. Generally they involved Parkinson-like symptoms which when first observed were usually mild to moderately severe and usually reversible. Other types of neuromuscular reactions (motor restlessness, dystonia, akathisia, hyperreflexia, opisthotonos, oculogyric crises) have been reported far less frequently, but were often more severe. Severe extrapyramidal reactions have been reported at relatively low doses. Generally, extrapyramidal symptoms are dose-related since they occur at relatively high doses and disappear or become less severe when the dose is reduced. Antiparkinson drugs may be required. Persistent extrapyramidal reactions have been reported and the drug may have to be discontinued in such cases. *Withdrawal Emergent Neurological Signs*—Abrupt discontinuation of short-term antipsychotic therapy is generally uneventful. However, some patients on maintenance treatment experience transient dyskinetic signs after abrupt withdrawal. In certain cases these are indistinguishable from "Tardive Dyskinesia" except for duration. It is unknown whether gradual withdrawal will reduce the occurrence of these signs, but until further evidence is available HALDOL should be gradually withdrawn. *Tardive Dyskinesia*—As with all antipsychotic agents HALDOL has been associated with persistent dyskinesias. Tardive dyskinesia, a syndrome consisting of potentially irreversible, involuntary, dyskinetic movements, may appear in some patients on long-term therapy or may occur after drug therapy has been discontinued. The risk appears to be greater in elderly patients on high-dose therapy, especially females. The symptoms are persistent and in some patients irreversible. The syndrome is characterized by rhythmical involuntary movements of tongue, face, mouth or jaw (e.g., protrusion of tongue, puffing of cheeks, puckering of mouth, chewing movements). Sometimes these may be accompanied by involuntary movements of extremities and the trunk. There is no known effective treatment for tardive dyskinesia; antiparkinson agents usually do not alleviate the symptoms of this syndrome. It is suggested that all antipsychotic agents be discontinued if these symptoms appear. Should it be necessary to reinstitute treatment, or increase the dosage of the agent, or switch to a different antipsychotic agent, this syndrome may be masked. It has been reported that fine vermicular movement of the tongue may be an early sign of tardive dyskinesia and if the medication is stopped at that time the full syndrome may not develop. *Tardive Dystonia*—Tardive dystonia, not associated with the above syndrome, has also been reported. Tardive dystonia is characterized by delayed onset of choreic or dystonic movements, is often persistent, and has the potential of becoming irreversible. *Other CNS Effects*—Insomnia, restlessness, anxiety, euphoria, agitation, drowsiness, depression, lethargy, headache, confusion, vertigo, grand mal seizures, and exacerbation of psychotic symptoms including hallucinations, and catatonic-like behavioral states which may be responsive to drug withdrawal and/or treatment with anticholinergic drugs.

*Body as a Whole:* Neuroleptic malignant syndrome (NMS), hyperpyrexia and heat stroke have been reported with HALDOL. (See WARNINGS for further information concerning NMS.) *Cardiovascular Effects:* Tachycardia, hypotension, hypertension and ECG changes. *Hematologic Effects:* Reports of mild, usually transient leukopenia and leukocytosis, minimal decreases in red blood cell counts, anemia, or a tendency toward lymphomonocytosis; agranulocytosis rarely reported and only in association with other medication. *Liver Effects:* Impaired liver function and/or jaundice. *Dermatologic Reactions:* Maculopapular and acneiform reactions, isolated cases of photosensitivity, loss of hair. *Endocrine Disorders:* Lactation, breast engorgement, mastalgia, menstrual irregularities, gynecomastia, impotence, increased libido, hyperglycemia, hypoglycemia and hyponatremia. *Gastrointestinal Effects:* Anorexia, constipation, diarrhea, hypersalivation, dyspepsia, nausea and vomiting. *Autonomic Reactions:* Dry mouth, blurred vision, urinary retention, diaphoresis, and priapism. *Respiratory Effects:* Laryngospasm, bronchospasm and increased depth of respiration. *Special Senses:* Cataracts, retinopathy and visual disturbances. *Other:* Cases of sudden and unexpected death have been reported in association with the administration of HALDOL. The nature of the evidence makes it impossible to determine definitively what role, if any, HALDOL played in the outcome of the reported cases. The possibility that HALDOL caused death cannot, of course, be excluded, but it is to be kept in mind that sudden and unexpected death may occur in psychotic patients when they go untreated or when they are treated with other antipsychotic drugs.

**IMPORTANT: Full directions for use should be read before HALDOL or HALDOL Decanoate products are administered or prescribed.**

**For information on symptoms and treatment of overdosage, see full prescribing information.**

The short-acting HALDOL injectable form is intended only for acutely agitated psychotic patients with moderately severe to very severe symptoms.

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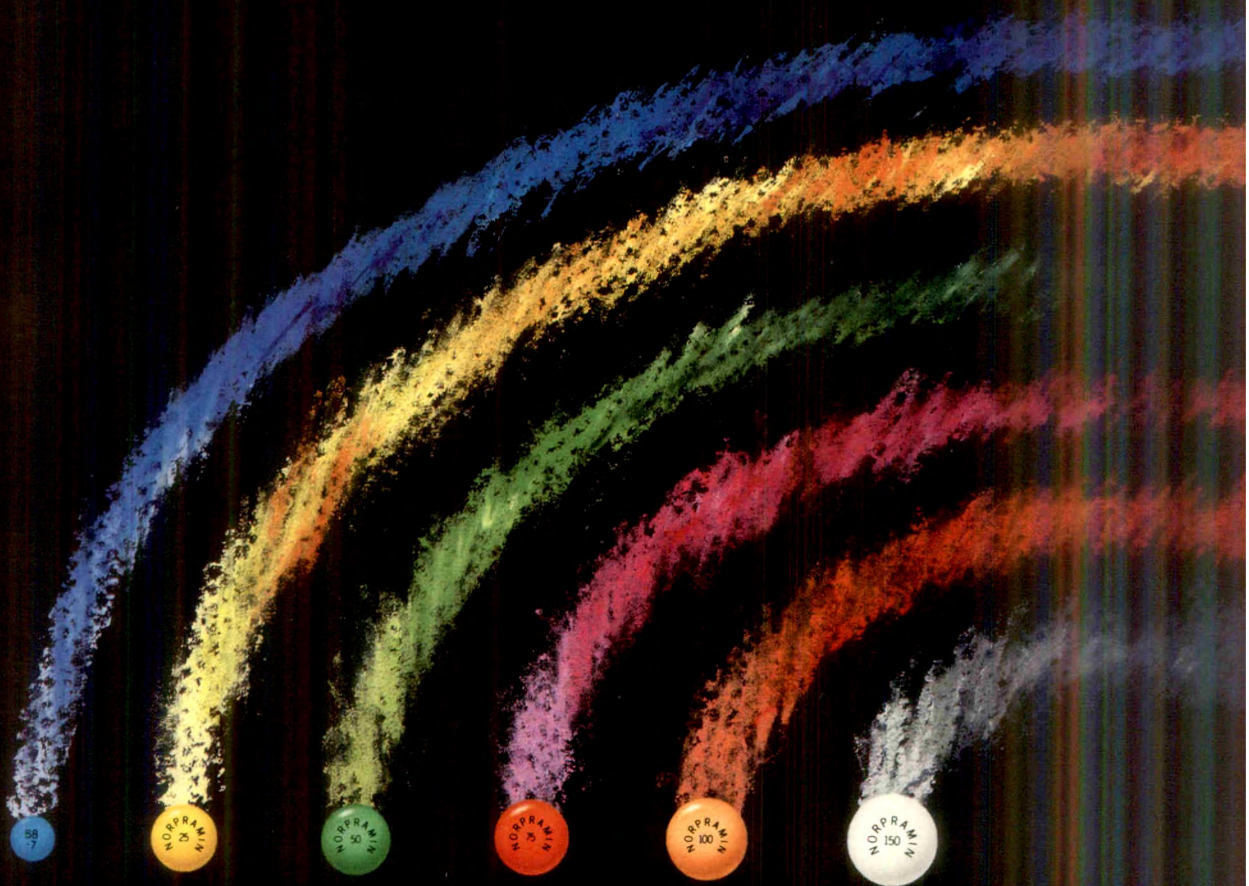

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(Brief Summary of Prescribing Information appears on the next page.)

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†Norpramin does not usually inhibit normal activity, although patients should be cautioned against driving or operating machinery if drowsiness occurs (see Warnings, Precautions, and Adverse Reactions).

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8-1912 (NR081) February, 1989 Printed in U.S.A.

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# Norpramin® 10, 25, 50, 75, 100, 150 mg

(desipramine hydrochloride tablets USP)

## Norpramin®

(desipramine hydrochloride tablets USP)

### BRIEF SUMMARY

CAUTION: Federal law prohibits dispensing without prescription.

### INACTIVE INGREDIENTS

The following inactive ingredients are contained in all dosage strengths: acacia, calcium carbonate, corn starch, D&C Red No. 30 and D&C Yellow No. 10 (except 10 mg and 150 mg), FD&C Blue No. 1, FD&C Red No. 3, FD&C Yellow No. 6, hydrogenated soy oil, iron oxide, light mineral oil, magnesium stearate, mannitol, polyethylene glycol 8000, pregelatinized corn starch, sodium benzoate (except 150 mg), sucrose, talc, titanium dioxide, and other ingredients.

### CLINICAL PHARMACOLOGY

*Metabolism*

The rate of metabolism of tricyclic antidepressants varies widely from individual to individual, chiefly on a genetically determined basis. In general, the elderly metabolize tricyclic antidepressants more slowly than do younger adults.

Certain drugs, particularly the psychostimulants and the phenothiazines, increase plasma levels of concomitantly administered tricyclic antidepressants through competition for the same metabolic enzyme systems. Other substances, particularly barbiturates and alcohol, induce liver enzyme activity and thereby reduce tricyclic antidepressant plasma levels. Similar effects have been reported with tobacco smoke.

Additional information on metabolism appears in Full Prescribing Information.

### CONTRAINDICATIONS

Desipramine hydrochloride should not be given in conjunction with, or within 2 weeks of, treatment with an MAO inhibitor drug; hyperpyretic crises, severe convulsions, and death have occurred in patients taking MAO inhibitors and tricyclic antidepressants. When Norpramin (desipramine hydrochloride) is substituted for an MAO inhibitor, at least 2 weeks should elapse between treatments. Norpramin should then be started cautiously and should be increased gradually.

The drug is contraindicated in the acute recovery period following myocardial infarction. It should not be used in those who have shown prior hypersensitivity to the drug. Cross sensitivity between this and other dibenzazepines is a possibility.

### WARNINGS

1. Extreme caution should be used when this drug is given in the following situations:
   a. In patients with cardiovascular disease, because of the possibility of conduction defects, arrhythmias, tachycardias, strokes, and acute myocardial infarction.
   b. In patients with a history of urinary retention or glaucoma, because of the anticholinergic properties of the drug.
   c. In patients with thyroid disease or those taking thyroid medication, because of the possibility of cardiovascular toxicity, including arrhythmias.
   d. In patients with a history of seizure disorder, because this drug has been shown to lower the seizure threshold.
2. This drug is capable of blocking the antihypertensive effect of guanethidine and similarly acting compounds.
3. **USE IN PREGNANCY**
   Safe use of desipramine hydrochloride during pregnancy and lactation has not been established; therefore, if it is to be given to pregnant patients, nursing mothers, or women of childbearing potential, the possible benefits must be weighed against the possible hazards to mother and child. Animal reproductive studies have been inconclusive.
4. **USE IN CHILDREN**
   Norpramin (desipramine hydrochloride) is not recommended for use in children since safety and effectiveness in the pediatric age group have not been established. (See ADVERSE REACTIONS, Cardiovascular.)
5. The patient should be cautioned that this drug may impair the mental and/or physical abilities required for the performance of potentially hazardous tasks such as driving a car or operating machinery.
6. In patients who may use alcohol excessively, it should be borne in mind that the potentiation may increase the danger inherent in any suicide attempt or overdosage.

### PRECAUTIONS

1. It is important that this drug be dispensed in the least possible quantities to depressed outpatients, since suicide has been accomplished with this class of drug. Ordinary prudence requires that children not have access to this drug or to potent drugs of any kind; if possible, this drug should be dispensed in containers with child-resistant safety closures. Storage of this drug in the home must be supervised responsibly.
2. If serious adverse effects occur, dosage should be reduced or treatment should be altered.
3. Norpramin (desipramine hydrochloride) therapy in patients with manic-depressive illness may induce a hypomanic state after the depressive phase terminates.
4. The drug may cause exacerbation of psychosis in schizophrenic patients.
5. Close supervision and careful adjustment of dosage are required when this drug is given concomitantly with anticholinergic or sympathomimetic drugs.
6. Patients should be warned that while taking this drug their response to alcoholic beverages may be exaggerated.
7. Clinical experience in the concurrent administration of ECT and antidepressant drugs is limited. Thus, if such treatment is essential, the possibility of increased risk relative to benefits should be considered.
8. If Norpramin (desipramine hydrochloride) is to be combined with other psychotropic agents such as tranquilizers or sedative/hypnotics, careful consideration should be given to the pharmacology of the agents employed since the sedative effects of Norpramin and benzodiazepines (e.g., chlordiazepoxide or diazepam) are additive. Both the sedative and anticholinergic effects of the major tranquilizers are also additive to those of Norpramin.
9. Concurrent administration of cimetidine and tricyclic antidepressants can produce clinically significant increases in the plasma levels of the tricyclic antidepressants. Conversely, decreases in plasma levels of the tricyclic antidepressants have been reported upon discontinuation of cimetidine which may result in the loss of the therapeutic efficacy of the tricyclic antidepressant.
10. This drug should be discontinued as soon as possible prior to elective surgery because of the possible cardiovascular effects. Hypertensive episodes have been observed during surgery in patients taking desipramine hydrochloride.
11. Both elevation and lowering of blood sugar levels have been reported.
12. Leukocyte and differential counts should be performed in any patient who develops fever and sore throat during therapy; the drug should be discontinued if there is evidence of pathologic neutrophil depression.

### ADVERSE REACTIONS

Note: Included in the following listing are a few adverse reactions that have not been reported with this specific drug. However, the pharmacologic similarities among the tricyclic antidepressant drugs require that each of the reactions be considered when Norpramin (desipramine hydrochloride) is given.

*Cardiovascular:* hypotension, hypertension, tachycardia, palpitation, arrhythmias, heart block, myocardial infarction, stroke. There has been a report of an "acute collapse" and "sudden death" in an eight-year old (18 kg) male, treated for two years for hyperactivity (See WARNINGS, Use in Children.)

*Psychiatric:* confusional states (especially in the elderly) with hallucinations, disorientation, delusions; anxiety, restlessness, agitation; insomnia and nightmares; hypomania exacerbation of psychosis.

*Neurologic:* numbness, tingling, paresthesias of extremities; incoordination, ataxia tremors; peripheral neuropathy; extrapyramidal symptoms; seizures; alteration in EE patterns; tinnitus.

*Anticholinergic:* dry mouth, and rarely associated sublingual adenitis; blurred vision disturbance of accommodation, mydriasis, increased intraocular pressure; constipation paralytic ileus; urinary retention, delayed micturition, dilatation of urinary tract.

*Allergic:* skin rash, petechiae, urticaria, itching, photosensitization (avoid excessiv exposure to sunlight), edema (of face and tongue or general), drug fever, cross sensitivit with other tricyclic drugs.

*Hematologic:* bone marrow depressions including agranulocytosis, eosinophilia, purpura thrombocytopenia.

*Gastrointestinal:* anorexia, nausea and vomiting, epigastric distress, peculiar taste abdominal cramps, diarrhea, stomatitis, black tongue.

*Endocrine:* gynecomastia in the male, breast enlargement and galactorrhea in the female increased or decreased libido, impotence, painful ejaculation, testicular swelling elevation or depression of blood sugar levels; syndrome of inappropriate antidiureti hormone secretion (SIADH).

*Other:* jaundice (simulating obstructive), altered liver function; weight gain or loss perspiration, flushing; urinary frequency, nocturia; parotid swelling; drowsiness, dizziness weakness and fatigue, headache; alopecia.

*Withdrawal Symptoms:* Though not indicative of addiction, abrupt cessation of treatmen after prolonged therapy may produce nausea, headache, and malaise.

### OVERDOSAGE

There is no specific antidote for desipramine, nor are there specific phenomena o diagnostic value characterizing poisoning by the drug.

Within an hour of ingestion the patient may become agitated or stuporous and the comatose. Hypotension, shock, and renal shutdown may ensue. Grand mal seizures, bot early and late after ingestion, have been reported. Hyperactive reflexes, hyperpyrexia muscle rigidity, vomiting, and ECG evidence of impaired conduction may occur. Serious disturbances of cardiac rate, rhythm, and output can occur. The precepts of early evacuatio of the ingested material and subsequent support of respiration (airway and movement) circulation, and renal output apply.

The principles of management of coma and shock by means of the mechanical respirator cardiac pacemaker, monitoring of central venous pressure, and regulation of fluid and acid-base balance are well known in most medical centers and are not further discussed here. Because CNS involvement, respiratory depression, and cardiac arrhythmia can occu suddenly, hospitalization and close observation are generally advisable, even when the amount ingested is thought to be small or the initial degree of intoxication appears slight o moderate. Most patients with ECG abnormalities should have continuous cardiac monitoring for at least 72 hours and be closely observed until well after cardiac status has returned t normal; relapses may occur after apparent recovery.

The slow intravenous administration of physostigmine salicylate has been reported t reverse most of the anticholinergic cardiovascular and CNS effects of overdose wit tricyclic antidepressants. In adults, 1 to 3 mg has been reported to be effective. In children the dose should be started with 0.5 mg and repeated at 5-minute intervals to determine th minimum effective dose; no more than 2 mg should be given. Because of the short duratio of action of physostigmine, the effective dose should be repeated at 30-minute to 60 minute intervals, as necessary. Rapid injection should be avoided to reduce the possibilit of physostigmine-induced convulsions.

Other possible therapeutic considerations include:

(a) Dialysis: Desipramine is found in low concentration in the serum, even after massive oral dose. In vitro experiments in which blood bank blood was used indicat that it is very poorly dialyzed. Because of indications that the drug is secreted i gastric juice, constant gastric lavage has been suggested.

(b) Pharmacologic treatment of shock: Since desipramine potentiates the action c such vasopressor agents as levarterenol and metaraminol, they should be used onl with caution.

(c) Pharmacologic control of seizures: Intravenous barbiturates are the treatment c choice for the control of grand mal seizures. One may, alternatively, consider th parenteral use of diphenylhydantoin, which has less central depressant effect bu also has an effect on heart rhythm that has not yet been fully defined.

(d) Pharmacologic control of cardiac function: Severe disturbances of cardiac rate rhythm, and output are probably the initiating events in shock. Intravascular volum must be maintained by i.v. fluids. Digitalization should be carried out early in vie of the fact that a positive inotropic effect can be achieved without increase i cardiac work. Many of the cardiodynamic effects of digitalis are the exact opposit of those of massive doses of desipramine (animal studies).

Product Information as of January, 1989 Y398D

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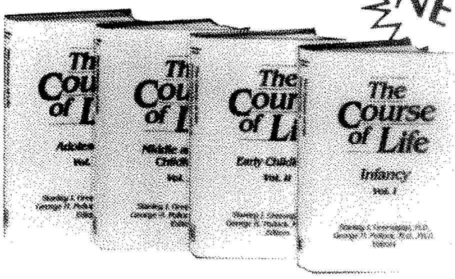

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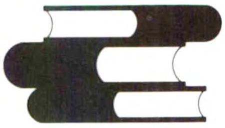

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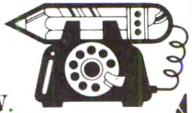

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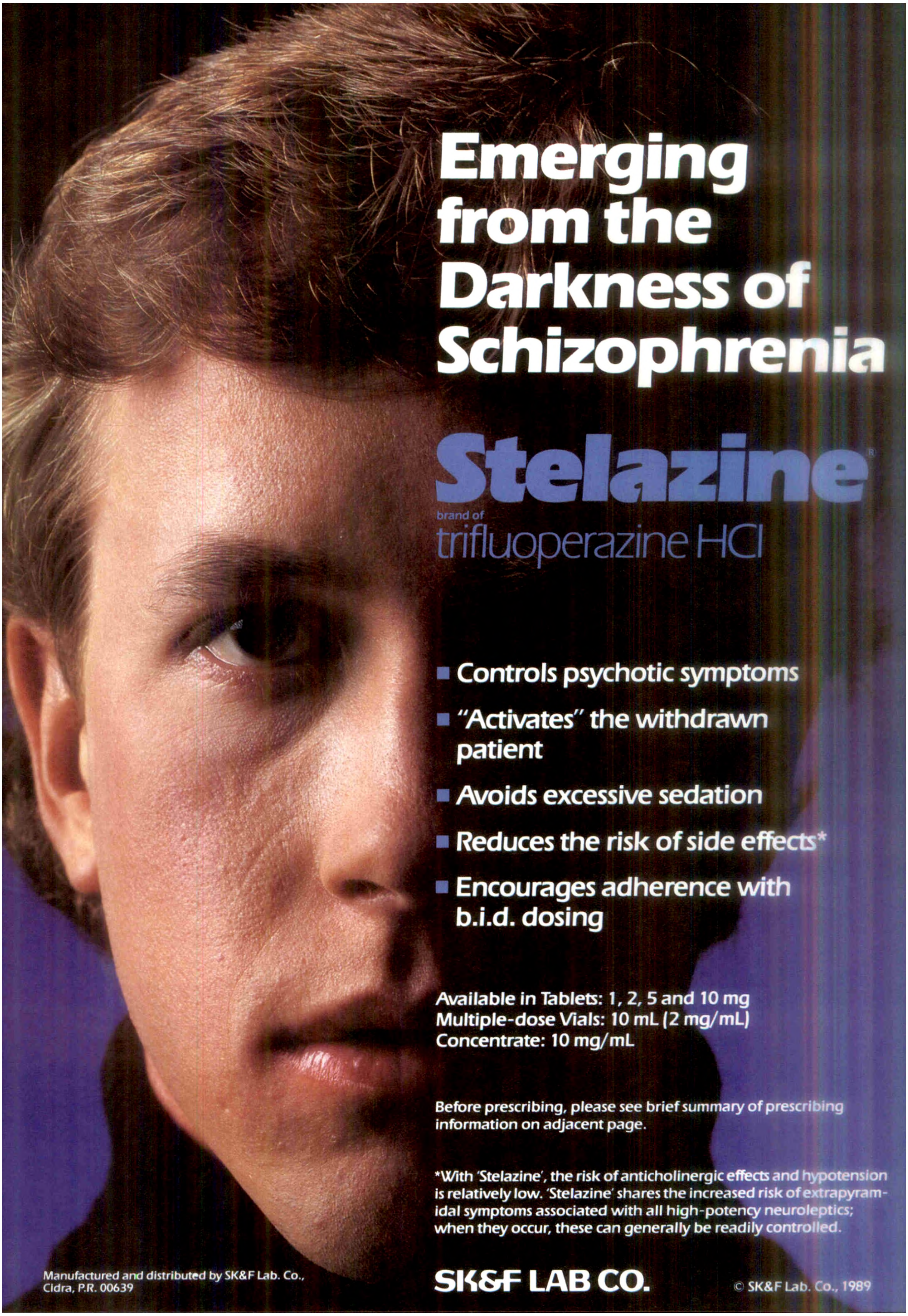

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brand of
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- Controls psychotic symptoms
- "Activates" the withdrawn patient
- Avoids excessive sedation
- Reduces the risk of side effects*
- Encourages adherence with b.i.d. dosing

Available in Tablets: 1, 2, 5 and 10 mg
Multiple-dose Vials: 10 mL (2 mg/mL)
Concentrate: 10 mg/mL

Before prescribing, please see brief summary of prescribing information on adjacent page.

*With 'Stelazine', the risk of anticholinergic effects and hypotension is relatively low. 'Stelazine' shares the increased risk of extrapyramidal symptoms associated with all high-potency neuroleptics; when they occur, these can generally be readily controlled.

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**SK&F LAB CO.**

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**Stelazine**® brand of

trifluoperazine HCl

**Before prescribing, see complete prescribing information in SK&F Lab Co. literature or PDR. The following is a brief summary.**

**Contraindications:** Comatose or greatly depressed states due to C.N.S. depressants, blood dyscrasias; bone marrow depression; liver damage.

**Warnings:** Tardive dyskinesia (TD) may develop in patients treated with neuroleptic (antipsychotic) drugs. The risk of TD and likelihood of irreversibility are thought to increase as duration of treatment and total cumulative neuroleptic dose increase. Much less commonly, the syndrome can develop after relatively brief treatment at low doses. There is no known treatment for TD, although it may remit if neuroleptics are withdrawn. Neuroleptic treatment may suppress signs and symptoms of the syndrome and thereby mask the underlying disease process. To minimize risk of TD, generally reserve chronic neuroleptic treatment for patients who suffer from chronic illness that responds to neuroleptics and for whom alternative, effective, less harmful treatments are not available or appropriate. In patients requiring chronic treatment, the minimal effective dose and shortest duration of treatment should be sought. Periodically reassess need for continued treatment. If signs and symptoms of TD appear, discontinuation of neuroleptics should be considered. (See PRECAUTIONS.)

Neuroleptic Malignant Syndrome (NMS), a potentially fatal symptom complex, has been reported in association with antipsychotic drugs. Clinical manifestations include: Hyperpyrexia, muscle rigidity, altered mental status and evidence of autonomic instability.

The management of NMS should include 1) immediate discontinuation of antipsychotic drugs and other drugs not essential to concurrent therapy, 2) intensive symptomatic treatment and medical monitoring, and 3) treatment, if available, of any concomitant serious medical problems.

'Stelazine' Concentrate contains sodium bisulfite, which may cause allergic-type reactions including anaphylactic symptoms or asthmatic episodes in certain susceptible people. The prevalence of sulfite sensitivity in the general population is unknown and probably low and is seen more frequently in asthmatic than in non-asthmatic people.

Generally avoid using in patients hypersensitive (e.g., have had blood dyscrasias, jaundice) to any phenothiazine. Caution patients about activities requiring alertness (e.g., operating vehicles or machinery), especially during the first few days' therapy. Additive depressant effect is possible with other C.N.S. depressants, including alcohol. Do not use in pregnancy except when essential and potential benefits clearly outweigh possible hazards. Prolonged jaundice, extrapyramidal signs, hyperreflexia and hyporeflexia have been reported in newborns whose mothers received phenothiazines. There is evidence that phenothiazines are excreted in the breast milk of nursing mothers.

**Precautions:** Since some patients chronically exposed to neuroleptics will develop tardive dyskinesia, it is advised that, if possible, full information about this risk be given to patients or their guardians when chronic use is contemplated.

Use cautiously in angina. Avoid high doses and parenteral use when cardiovascular system is impaired since hypotension has occurred. Antiemetic effect may mask the signs of overdosage of other drugs or obscure diagnosis and treatment of certain physical disorders. Prolonged use of high doses may result in cumulative effects with severe C.N.S. or vasomotor symptoms. If retinal changes occur, discontinue drug. Agranulocytosis, thrombocytopenia, pancytopenia, anemia, cholestatic jaundice, liver damage have been reported. Use cautiously in patients with glaucoma.

Patients with a history of long-term therapy with 'Stelazine' and/or other neuroleptics should be evaluated periodically for possible dosage adjustment or discontinuance of drug therapy. Neuroleptic drugs cause elevated prolactin levels that persist during chronic use. Since approximately one-third of human breast cancers are prolactin-dependent in vitro, this elevation is of potential importance if neuroleptic drug use is contemplated in a patient with a previously detected breast cancer. However, clinical and epidemiologic studies to date have not shown an association between the chronic use of neuroleptic drugs and mammary tumorigenesis. Chromosomal aberrations in spermatocytes and abnormal sperm have been demonstrated in rodents treated with certain neuroleptics. Use cautiously in persons who will be exposed to extreme heat.

Phenothiazines may diminish the effect of oral anticoagulants. Phenothiazines can produce alpha-adrenergic blockade. Concomitant use of phenothiazines with propranolol increases plasma levels of both drugs. Concurrent use of phenothiazines may counteract antihypertensive effects of guanethidine and related compounds. Thiazide diuretics may accentuate the orthostatic hypotension that may occur with phenothiazines. Phenothiazines may lower the convulsive threshold and may also precipitate phenytoin toxicity; dosage adjustments of anticonvulsants may be necessary. If neuromuscular reactions occur in pregnant women, or in children, permanently stop neuroleptic therapy. Patients should not receive 'Stelazine' 48 hours before or 24 hours after myelography with the contrast medium metrizamide. The presence of phenothiazines may produce false positive phenylketonuria (PKU) test results.

**Adverse Reactions:** Drowsiness, dizziness, skin reactions, rash, dry mouth, insomnia, amenorrhea, fatigue, muscular weakness, anorexia, lactation, blurred vision. Neuromuscular (extrapyramidal) reactions: motor restlessness, dystonias, pseudo-parkinsonism, tardive dyskinesia, and a variant, tardive dystonia.

**Other adverse reactions reported with Stelazine (trifluoperazine HCl, SK&F) or other phenothiazines:** Some adverse effects are more frequent or intense in specific disorders (e.g., mitral insufficiency or pheochromocytoma).

Grand mal and petit mal convulsions, particularly in the presence, or with history, of EEG abnormalities; altered cerebrospinal fluid proteins; cerebral edema; prolongation and intensification of the action of C.N.S. depressants, atropine, heat, and organophosphorus insecticides; nasal congestion, headache, nausea, constipation, obstipation, adynamic ileus, ejaculatory disorders/impotence, priapism, atonic colon, urinary retention, miosis and mydriasis; reactivation of psychotic processes, catatonic-like states, hypotension (sometimes fatal); cardiac arrest; leukopenia, eosinophilia, pancytopenia, agranulocytosis, thrombocytopenic purpura, hemolytic anemia, aplastic anemia, jaundice, biliary stasis, hyperglycemia, hypoglycemia, glycosuria, menstrual irregularities, galactorrhea, gynecomastia, false positive pregnancy tests, photosensitivity, itching, erythema, urticaria, eczema up to exfoliative dermatitis, asthma, laryngeal edema, angioneurotic edema, anaphylactoid reactions, peripheral edema; reversed epinephrine effect; hyperpyrexia; mild fever after large I.M. doses; increased appetite; increased weight; a systemic lupus erythematosus-like syndrome; pigmentary retinopathy; with prolonged administration of substantial doses, skin pigmentation, epithelial keratopathy, and lenticular and corneal deposits; neuroleptic malignant syndrome, which may be fatal; EKG changes—particularly nonspecific, usually reversible Q and T wave distortions—have been observed. Temporary nausea, vomiting, dizziness, and tremulousness may follow abrupt cessation of high-dose therapy. NOTE: Sudden death in patients taking phenothiazines (apparently due to cardiac arrest or asphyxia due to failure of cough reflex) has been reported.

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**INDICATIONS:** Management of anxiety disorders, or short-term relief of symptoms of anxiety. Anxiety or tension associated with the stress of everyday life usually does not require treatment with an anxiolytic. Symptomatic relief of acute agitation, tremor, delirium tremens and hallucinosis due to acute alcohol withdrawal; adjunctively in skeletal muscle spasm due to reflex spasm to local pathology; spasticity caused by upper motor neuron disorders; athetosis; stiff-man syndrome; convulsive disorders (not as sole therapy).
The effectiveness of Valium in long-term use, that is, more than 4 months, has not been assessed by systematic clinical studies. The physician should periodically reassess the usefulness of the drug for the individual patient.
**CONTRAINDICATED:** Known hypersensitivity to the drug. Children under 6 months of age. Acute narrow angle glaucoma; may be used in patients with open angle glaucoma who are receiving appropriate therapy.
**WARNINGS:** Not of value in psychotic patients. Caution against hazardous occupations requiring complete mental alertness. When used adjunctively in convulsive disorders, possibility of increase in frequency and/or severity of grand mal seizures may require increased dosage of standard anticonvulsant medication; abrupt withdrawal may be associated with temporary increase in frequency and/or severity of seizures. Advise against simultaneous ingestion of alcohol and other CNS depressants.
***Usage in Pregnancy:* Use of minor tranquilizers during first trimester should almost always be avoided because of increased risk of congenital malformations as suggested in several studies. Consider possibility of pregnancy when instituting therapy; advise patients to discuss therapy if they intend to or do become pregnant.**
Withdrawal symptoms of the barbiturate type have occurred after discontinuation of benzodiazepines (see Drug Abuse and Dependence).
**PRECAUTIONS:** If combined with other psychotropics or anticonvulsants, consider carefully pharmacology of agents employed; drugs such as phenothiazines, narcotics, barbiturates, MAO inhibitors and other antidepressants may potentiate its action. Usual precautions indicated in patients severely depressed, or with latent depression, or with suicidal tendencies. Observe usual precautions in impaired renal or hepatic function. Limit dosage to smallest effective amount in elderly and debilitated to preclude ataxia or oversedation.
The clearance of Valium and certain other benzodiazepines can be delayed in association with Tagamet (cimetidine) administration. The clinical significance of this is unclear. Inform patients to consult physician before increasing dose or abruptly discontinuing diazepam.
**SIDE EFFECTS:** Drowsiness, confusion, diplopia, hypotension, changes in libido, nausea, fatigue, depression, dysarthria, jaundice, skin rash, ataxia, constipation, headache, incontinence, changes in salivation, slurred speech, tremor, vertigo, urinary retention, blurred vision. Paradoxical reactions such as acute hyperexcited states, anxiety, hallucinations, increased muscle spasticity, insomnia, rage, sleep disturbances, stimulation have been reported; should these occur, discontinue drug. Isolated reports of neutropenia, jaundice; periodic blood counts and liver function tests advisable during long-term therapy.
*Drug Abuse and Dependence:* Withdrawal symptoms similar to those noted with barbiturates and alcohol have occurred following abrupt discontinuation of diazepam; more severe seen after excessive doses over extended periods; milder after taking continuously at therapeutic levels for several months. After extended therapy, avoid abrupt discontinuation and taper dosage. Carefully supervise addiction-prone individuals because of predisposition to habituation and dependence.
**DOSAGE:** Individualize for maximum beneficial effect. *Adults:* Anxiety disorders, symptoms of anxiety, 2 to 10 mg b.i.d. to q.i.d.; alcoholism, 10 mg t.i.d. or q.i.d. in first 24 hours, then 5 mg t.i.d. or q.i.d. as needed; adjunctively in skeletal muscle spasm, 2 to 10 mg t.i.d. or q.i.d.; adjunctively in convulsive disorders, 2 to 10 mg b.i.d. to q.i.d. *Geriatric or debilitated patients:* 2 to 2½ mg, 1 or 2 times daily initially, increasing as needed and tolerated (See Precautions.) *Children:* 1 to 2½ mg t.i.d. or q.i.d. initially, increasing as needed and tolerated (not for use under 6 months).
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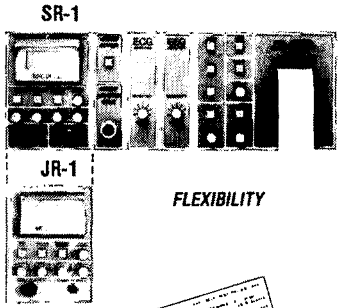

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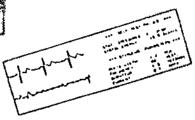

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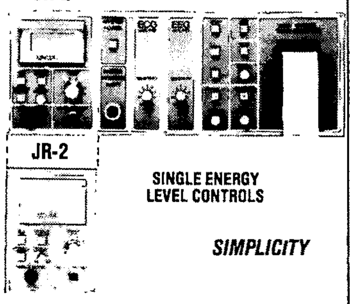

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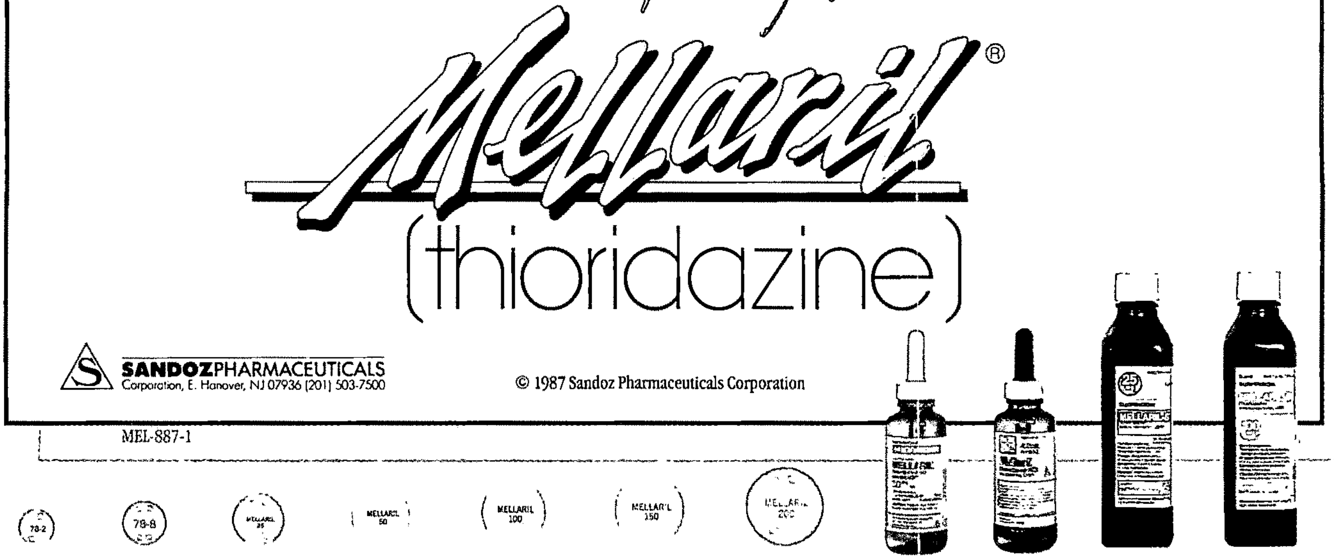

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*Editorial*

# New Year's Greetings

"History," said a witty historian, whose name eludes our failing memory, "is just one damn thing after another." As we watch the endless flow across our editorial desk of manuscripts addressing in disjointed confusion the myriad facets of psychiatric endeavors, we can only concur in that despairing judgment. Were it not for our many colleagues whose devoted service as reviewers helps us to decide what is new, true, and publishable, we might sink beneath the flood. They are our alprazolam, our nortriptyline, our haloperidol, our constant moral support, and it is with heartfelt pleasure that we express our gratitude for their wise and ungrudging contributions to our editorial work during the period from November 1, 1988, to October 31, 1989.

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The Editor is deeply grateful to the members of his Editorial Board for their help and counsel during a year that brought the sad loss of the *Journal*'s Deputy Editor, Dr. Morris A. Lipton, whose death in the spring of the year deprived us of a friend and a scholar. We are especially thankful to Dr. Nancy C. Andreasen for her willingness to expand her activities as Book Forum Editor to include those of Deputy Editor, a position that she assumed officially during the fall. The year has also seen the departure of four devoted Associate Editors who completed the second of their two four-year terms in May of 1989. Drs. Ross Baldessarini, Elissa Benedek, Herbert Meltzer, and Lorraine Siggins all served the *Journal* with wisdom and grace; their loss is mitigated by our good fortune in welcoming Drs. Paula Clayton, Arnold Cooper, Howard Goldman, and David Kupfer to the *Journal*'s Editorial Board.

The Editor must take particular note of the innovations in the *Journal*'s procedures introduced during the year by his Managing Editor, Ms. Melanie Shipley, and Ms. Linda Loy, Assistant Managing Editor. Along with their dedicated Editorial staff they have significantly expedited the processing and publication of *Journal* manuscripts.

Like every other aspect of medicine as a profession, the editing of a professional journal becomes administratively more complex with each passing year. The Medical Director, Dr. Melvin Sabshin, has been an invaluable pilot through often perilous waters, and the Editor is deeply appreciative of his guidance and of the support that he and the Board of Trustees have consistently provided him. And he must also express his sincere thanks for their many contributions to the *Journal*'s health and welfare to Drs. Robert J. Campbell III, John Hamilton, William A. More, Harold A. Pincus, Carolyn B. Robinowitz, Jeanne Spurlock, John A. Talbott, and Jack W. White; to Mses. Laura Abedi, Teddye Clayton, Carol Davis, Nancy Frey, Zing Jung, Joan Lefkowitz, Karen Loper, Brenda Overman, and Beth Prester; and to Messrs. John Blamphin, George Campbell, Herbert M. Gant, Steve Jones, Joel Klein, Terry Light, Ronald McMillen, and Raymond J. Purkis, Jr.

The 1990s are upon us—Happy New Year!

J.C.N.

# Psychotherapy Training for the Psychiatrist of the Future

Paul C. Mohl, M.D., James Lomax, M.D., Allan Tasman, M.D., Carlyle Chan, M.D., William Sledge, M.D., Paul Summergrad, M.D., and Malkah Notman, M.D.

*There is uncertainty about the future role of psychodynamic psychotherapy in psychiatric practice and education. The Association for Academic Psychiatry and the American Association of Directors of Psychiatry Residency Training formed a joint task force to review the issue. It developed a rationale for continued training in expressive psychotherapy and a model curriculum for such training that is both effective and realistic in terms of the diverse demands and structures of modern residencies. A minimum curriculum was also designed for resource-poor programs.*

(Am J Psychiatry 1990; 147:7–13)

The place of psychodynamic psychotherapy in modern psychiatric treatment is changing; it was the central modality during the 1950s but is now only one of several treatment skills that psychiatrists may possess. Its exact role in future practice and training has been a point of discussion, and in recent years there have been public debates at the APA annual meeting on the subject. Invariably, the neurobiologists seem less radical than the dynamicists fear, and the psychodynamic psychiatrists are far less dualistic and threatened than the biological people imagine. Nonetheless, one can still hear that psychiatrists should not be practicing psychotherapy any more or, conversely, that psychiatry is "losing the mind" (1). At stake is our vision of the future psychiatrist. Do we think the future psychiatrist should/will be an applied neurobiologist who should know only the *indications* for exploratory psychotherapy, so as to make appropriate referrals to psychologists and social workers, as many neurologists and family practitioners now do? Do we think that the remarkable new knowledge in neurobiology, including such areas as personality disorders (2), will render psychotherapy obsolete? Do we think that a psychiatrist poorly versed in psychotherapeutic perspectives will be at a competitive disadvantage with other mental health professionals? What effects do we think the radical economic restructuring of American medicine and mental health will have on patterns of practice? We are clearly at a historic scientific watershed, but should the psychiatrists who teach psychodynamic psychotherapy be viewed as the medieval alchemists and astrologers, only grudgingly giving way to the Newtons and Galileos of neurobiology, or should they be regarded as the medieval monks carefully preserving the writings of Aristotle lest the wisdom be lost?

Psychiatric educators, always guessing the future so they can prepare young psychiatrists for it, are particularly concerned with this issue. The choices they make will at the same time influence the answers to these questions and lay the groundwork for the future success or failure of the field, depending on how prescient the guesses turn out to be. Psychiatric educators are as uncertain as everyone else. Two recent studies highlighted the uncertainty. One (3), a survey of attitudes and opinions among department chairpersons, residency training directors, and practitioners, found that knowledge of psychodynamic theory and its application to such skills as countertransference management and psychodynamically informed supportive therapy was viewed as central to the training of all psychiatrists by over 90% of the respondents. However, specific knowledge about and skill in doing expressive psychotherapy was less valued.

Similarly, a survey (4) of current programs showed that many programs are carefully preserving a place

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for psychodynamic psychotherapy but that this place is far smaller than before. Most programs offer such training during outpatient rotations, which average 9 months and occupy three-fourths of the resident's time during postgraduate year 3 (PGY-3). Usually a couple of hours are available to continue following patients beyond the rotation, but it is unusual for a resident to be able to treat a patient longer than 18 months. Further, the teaching and supervising of long-term psychodynamic psychotherapy is increasingly relegated to part-time unpaid clinical faculty. Thus, the primary role models for residents do not necessarily convey the sense that psychodynamic psychotherapy is part of every psychiatrist's identity no matter what his or her primary interest area is.

These trends led the Association for Academic Psychiatry and the American Association of Directors of Psychiatry Residency Training to form a joint task force to consider the case for the continued importance of training in psychodynamic psychotherapy in current general psychiatry education and to devise a realistic, reasonable model curriculum for it.

The group did not consider psychotherapy broadly but focused on long-term psychodynamic psychotherapy, concluding that addressing such modalities as group therapy, family therapy, cognitive therapy, and behavior therapy would obscure the task and diffuse the effort. Other therapies—for example, brief dynamic treatments and long-term supportive modalities—were seen as derivative from, and thereby educationally building on, individual expressive therapy. The focus of the group was on what has been variously called "expressive," "exploratory," "reconstructive," "psychodynamic," "psychoanalytic," or "insight-oriented" psychotherapy. After much discussion, the task force concluded that psychotherapy in which the goal is to explore, understand, and alter the inner experience of another human being is not only the best way, but perhaps the only way, to learn and consolidate various core concepts and experiences. It is only once these concepts have been consolidated that the technical questions of "What is support?" and "What is an appropriate brief focus?" can be effectively learned and implemented by residents.

The task force also did not consider specific modifications and modernizations of the traditional curriculum in psychodynamic psychotherapy. There have been exciting research developments in the study of psychodynamic psychotherapy—e.g., the development of manuals (5, 6) and the identification of useful tactics in treatment (7, 8)—that will affect its practice and should influence training, but the task force addressed only two questions: Should long-term individual psychodynamic psychotherapy continue to be a significant part of a psychiatric residency? and What should a modern curriculum contain given the diverse demands of training? In dealing with this latter question, the task force was intent on producing a curriculum that would be realistic and usable in virtually all programs, not an ideal that would be shelved because it was out of touch with day-to-day training realities. In the end, we developed two curricula: one that should be applicable to the vast majority of residencies and one that is a minimum for resource-poor programs. The rationale, model curriculum, and minimum curriculum were all reviewed by both the Association for Academic Psychiatry and the American Association of Directors of Psychiatry Residency Training.

## RATIONALE

The task force identified 10 major reasons for continuing to teach psychodynamic psychotherapy. The first three involve the acquisition of skills directly related to the delivery of psychodynamic psychotherapy to psychiatric patients. The next seven are related to the acquisition of skills, knowledge, and experience important to other aspects of psychiatric and medical clinical practice.

1. Psychodynamic psychotherapy is an effective treatment for many mental disorders, and all well-trained psychiatrists should be familiar with its principles and techniques and should achieve a basic level of competence.
2. Training in psychodynamic psychotherapy provides the resident with a unique opportunity for professional growth and development by promoting the full development of the skills of a complete psychiatrist.
3. Many nonmedical mental health professionals who are supervised by psychiatrists use psychodynamic psychotherapy; therefore, for the psychiatrist to responsibly supervise such work, he or she should possess basic psychotherapeutic competence.
4. The concepts of psychodynamic psychotherapy are intimately related to the psychological and social concepts of all doctor-patient relationships. The psychotherapeutically competent psychiatrist will be able to provide more effective consultation to medical colleagues and will be able to manage his or her own nonpsychotherapy doctor-patient relationships more effectively.
5. Psychodynamic psychotherapy training provides the resident with experiences that enhance learning about and management of other dyadic relationships within psychiatry, such as in supervision, consultation, and mental health administration.
6. Training in psychodynamic psychotherapy enhances basic interviewing expertise by providing the resident with an opportunity to observe longitudinally the course of psychopathological and normal mental phenomena present in an initial interview. This experience makes it possible for the resident to recognize emerging mental phenomena earlier, more accurately, and more confidently.
7. Training in psychodynamic psychotherapy provides the resident with an in-depth and longitudinal study of both conscious and unconscious mental functioning, which may be normal or pathological and which are related to the effort to change thinking, feel-

ing, and behavior. Such an effort requires an ongoing relationship between therapist and patient and involves the inevitable obstacles, resistances, strengths, and opportunities related to such an effort. Understanding these phenomena is essential to treatment planning and management of virtually all psychiatric disorders.

8. Psychodynamic psychotherapy allows observation of complex pathological and normal mental functioning over time. In so doing, it complements the observation of similar mechanisms in inpatient, consultation, and emergency room settings. Furthermore, it provides access to the primary material that forms the basis of general psychodynamic theory. As such, psychotherapy training enhances the learning of psychodynamics as a basic science within psychiatry.

9. Many ethical difficulties result from psychiatrists' problems in managing their feelings and reactions to patients. With its emphasis on the complex dyadic emotional interplay between psychiatrist and patient, psychodynamic psychotherapy training enhances psychiatrists' ability to anticipate, analyze, and avoid ethical dilemmas and transgressions.

10. Practicing psychodynamic psychotherapy forces the psychiatrist in training to observe, analyze, and attempt to understand extremely complex interactive phenomena. This enforces an intellectual rigor and discipline in observing behavior, developing hypotheses, and analyzing theories and data.

In these rationales, a clear philosophy was at work. The exciting developments in clinical neuroscience do not displace the importance of the experiential meanings that behavioral and mental phenomena have to patients. Some of the most promising developments in neuroscience are at the interface of mental experience and biochemical phenomena (9–13). Not only clinical experience but empirical data support the notion that the most effective treatment for many patients is the combination of psychotherapy and pharmacologic treatment (14). Although many psychiatrists may choose to delegate the psychological treatment to others, just as in the past many psychiatrists delegated the pharmacologic treatment to others, a solid grounding in those treatments is essential. In short, a deep, usable understanding and ability to apply clinically the concepts of a dynamic unconscious, transference/countertransference, and mental defense mechanisms is central to being an effective pharmacotherapist, behavior therapist, inpatient psychiatrist, consultation psychiatrist, psychotherapist, community psychiatrist, neuropsychiatrist, emergency psychiatrist, geriatric psychiatrist, and, perhaps, even a laboratory research psychiatrist.

How can these principles be taught effectively yet reasonably concisely in residencies as they now exist?

## THE MODEL CURRICULUM

Residency curriculum structure provides a coordinated set of experiences to develop the core knowledge and skills of psychiatrists. The task force developed the following core curriculum in individual psychotherapy; for each postgraduate year, it specifies terminal and enabling objectives for the resident, a set of learning experiences used by the resident to meet the objectives, and evaluation instruments for determining whether the resident has acquired the pertinent knowledge, skills, and attitudes. The learning experiences are divided into seminars, case conferences, supervision, and clinical care. The ideas of Jerry Lewis (15) were influential in the development of this curriculum.

### *PGY-1*

*Goals.* The resident should be able to conduct open-ended diagnostic psychiatric interviews that both generate adequate information for initial psychiatric assessment and enlist the patient in a collaborative manner to participate in treatment. The resident should be able to facilitate increasingly more personal revelations by the patient about interpersonal and intrapsychic experiences and the patient's subjective responses to the experiences. The resident should appreciate the importance of a detailed personal history as it relates to symptom development. The resident should make salient observations about the patient's relationships, including the doctor-patient relationship.

*Learning experiences.* The resident should perform a large number (at least 20–25) of initial interviews with a variety of patients and conduct a large number of follow-up interviews. Each resident should videotape one of his or her psychiatric interviews that will be viewed by a faculty member and members of the residency group. Each resident should interview a substantial number of psychiatric inpatients in front of faculty and other residents. Each resident should also see and critique videotape interviews conducted by faculty and should observe such interviews in person. In a seminar on psychiatric interviewing, the resident should be assigned a list of readings on both diagnostic and process aspects of the psychiatric interview.

Case conferences in the first postgraduate year should emphasize diagnosis and broad areas of treatment planning. The case conferences should include discussions, at least in general terms, of the role of supportive and expressive psychotherapy.

The emphasis in PGY-1 supervision is on consolidation of the resident's identity as a physician and psychiatrist rather than on psychotherapy. Supervision is used to deepen understanding of the patient's psychopathology and to begin introducing the resident to psychodynamic principles and the impact of physician behavior and communication on the patient.

Clinical care given by first-year residents emphasizes diagnosis, crisis intervention, pharmacotherapy, and extensive history taking and treatment planning. Residents follow hospitalized patients with a primary focus on understanding the natural course and resolution with treatment of major psychiatric illness, rather than the provision of psychotherapeutic treatment.

*Evaluation.* The relevant evaluation of PGY-1 residents covers psychiatric assessment and interviewing and the residents' ability to perform appropriate clinical intervention. The PGY-1 evaluation instrument should specify the skills and abilities under consideration.

### *PGY-2*

*Goals.* During the second year, the resident should develop an understanding of core psychodynamic concepts, become familiar with transference and countertransference phenomena, gain sophistication in observing the process of psychotherapy, and develop an understanding of the definitions and roles of key concepts and interventions in psychotherapy (e.g., therapeutic alliance, empathy, clarification, interpretation). The resident should learn to recognize the patient's emotional states and his or her own reactions that interfere with or facilitate deeper patient revelation. The resident should be able to vicariously experience the patient's feelings while maintaining separateness and to subsequently communicate empathic understanding. The resident should recognize that empathy enables the patient to feel understood. The resident should become aware of multiple meanings of symptoms, thoughts, and feelings through his or her understanding of the patient's relevant past experiences, current situations, and relationship to the therapist. The resident should be able to detect conflict in patient behavior or thought. By the end of the second postgraduate year, the resident should be able to establish a therapeutic contract, recognize defense and resistance, and coordinate psychotherapy with other interventions, including medications, with patients suffering from a wide variety of diagnostic conditions. The resident should be able to identify and deal effectively with emergent issues in therapy and use supervisory or consultative feedback in ongoing psychotherapeutic work.

*Learning experiences.* Seminars and case conferences during the second postgraduate year should provide ample opportunity both to learn the basic principles of psychodynamics and psychotherapy and to practice the elements of psychotherapy. Didactic seminars should review in detail the basic knowledge involved in core clinical concepts. It is extremely helpful to have the opportunity to review psychotherapy conducted by a senior psychotherapist, particularly with a patient who might otherwise be seen by a resident in the program. Watching edited videotapes of psychotherapy sessions and observing live sessions are both useful. In conferences that use videotape material of a senior psychiatrist, the presence of another faculty member with a somewhat different orientation or style enriches the opportunities for learning.

A structured introduction to psychotherapy skills is also useful. In such conferences, residents and faculty members are asked to respond to videotape and audiotape patient material. Early in the seminar those responses may be written, and subsequently they may be verbal. Eventually, seminar participants conduct videotaped interviews of patients or actors. Throughout the course of the seminar, the residents have opportunities to experiment with different responses and receive feedback from their peers and the faculty members about those responses.

Clinical care in the second postgraduate year largely involves hospitalized patients, but assignments should also include at least two patients for whom outpatient psychotherapy is the predominant or exclusive form of treatment. Optimally, these first patients will have sought treatment because of psychological conflict. There should be at least 2 hours of weekly individual supervision during the second postgraduate year.

*Evaluation.* In the second postgraduate year, the evaluation takes place in seminars, case conferences, and supervision. Seminar evaluations focus on the resident's ability to present concepts in a coherent manner that reflects understanding of the theoretical material involved. In experiential learning situations, such as the psychotherapy case conference, it is often more important to give extensive feedback and downplay formal written evaluation. Supervisors, however, should complete a narrative evaluation form that addresses the goals and objectives we have enumerated.

### *PGY-3*

*Goals.* By the end of the third postgraduate year, the resident should have been able to involve at least two patients in the middle phase of insight-oriented dynamic psychotherapy. The resident should be able to manage silence, anxiety, aggression, and seductive behavior by psychotherapy patients. The resident should appreciate the basic theoretical and technical differences among the major approaches to psychotherapy and have a more sophisticated appreciation of psychological development and multiple levels of psychological meaning. The resident should have the knowledge and skill to understand and establish a therapeutic alliance with a variety of patients. The resident should demonstrate competence with empathic functions in psychotherapy and deal with fee setting and collection in the outpatient clinic. The resident should recognize and deal with resistance, particularly positive or negative transference reactions, and acting out. The resident should be aware of countertransference responses and be able to put them to use in understanding patients. The resident should understand major dynamic themes in individual sessions and organizing themes over the course of therapy and should be able to identify progress and stalemates. The resident should be able to avoid competition, overidentification, and moralizing with patients and should understand mental mechanisms and defensive structure. The resident should be able to appreciate and learn from mistakes without counterproductive defensive responses. The resident should also begin to appreciate the importance of the various forms of therapy termination and anticipate difficulties that will emerge in the termination phase. The resident should be able to understand the role of character in the patient's participation in treatment.

*Learning experiences.* Seminars in the third postgraduate year should deepen and broaden the resident's sophistication about psychotherapy. A core textbook with a variety of assigned readings is one way to both provide a unifying structure for seminars and help the resident become familiar with a variety of core readings and essential principles.

Case conferences during the early part of PGY-3 should emphasize the problems inherent in engaging a broad variety of patients in psychotherapeutic treatment. It is also useful to have a continuous case conference, in which the progress in ongoing psychotherapy with one or two patients receives special attention.

Clinical care during PGY-3 consists of 4–7 psychotherapy hours per week and at least one patient who is seen more than once per week. These patients should represent diverse experiences in terms of gender, diagnosis, age, phase of life, developmental level, and cognitive style. Each resident should have 2 hours of individual supervision and at least 1 other hour for a case conference.

*Evaluation.* Again, evaluation takes place in seminars, case conferences, and individual supervision. Evaluation in the case conferences and seminars is based on the same principles as for PGY-2. In individual supervision, greater sophistication is expected of the resident during this year, which should be reflected in the evaluation guidelines.

### *PGY-4*

*Goals.* Goals for this year include development of the ability to function autonomously as a psychotherapist and the capacity for continuing educational growth and development. By the end of this year, the resident should also become proficient in at least one subspecialized psychotherapeutic technique, such as time-limited, group, family, behavioral, cognitive, or hypno- therapy.

*Learning experiences.* In PGY-4, there should be one seminar on advanced individual psychotherapy and one seminar that introduces the resident to a psychotherapeutic subspecialty (brief psychotherapy, hypnosis, cognitive therapy, sexual therapy, etc.). The individual psychotherapy seminar should help the resident relate psychotherapy to other forms of treatment and should emphasize management of the middle and termination phases of psychotherapy.

The case conferences during part of PGY-4 should include a second continuous case conference in which the residents describe ongoing individual psychotherapy. A case conference emphasizing a particular psychotherapy subspecialty should also be offered and focus on the practice and evaluation of that form of therapy.

In PGY-4, most residents will not add new long-term cases but will add cases that provide the opportunity to use a subspecialty form of psychotherapy. There should be some unsupervised cases during this year. Each resident should have at least two individual supervisors in addition to participating in the case conferences.

*Evaluation.* The evaluation of PGY-4 residents should include an assessment of their ability to terminate therapy and to ask for consultation in psychotherapy.

In PGY-1, no more than 2 hours per week are required for activities exclusively related to this curriculum. In PGY-2, this increases to 6 hours per week: 1 hour of didactic seminar, 1 hour for the case conference, 2 hours of psychotherapy, and 2 hours of supervision. In PGY-3, the time needed for this curriculum peaks at approximately 8–11 hours per week: 1 hour of didactic seminar, 1 hour for the case conference, 2 hours of supervision, and 4–7 hours of cases. There would probably be a slight drop in hours in PGY-4 as the cases terminate and the didactic seminars become more episodic.

The task force emphasized the cumulative nature of training in expressive psychotherapy, which makes the consolidating experiences of PGY-4 especially important. Besides the incremental addition of specific knowledge and clinical skills, the cumulative and transforming nature of the experience produces a depth of understanding by the time of graduation so the way a psychodynamically informed psychiatrist hears patients is radically different from how he or she heard them in PGY-1.

## *Specific Considerations*

It is worth noting what is not included in this curriculum. The task force did not recommend personal psychotherapy for residents, individual work with a latency-age child, more cases, a specific structure (e.g., many thought there should be an outpatient rotation in PGY-2), more activities during PGY-1, or specific activities for rotations in settings involving other specific teaching tasks (e.g., consultation-liaison, inpatient units, emergency room).

In general, we were convinced that what should be expected of all residents and what is optimal could not be identical and, further, that our proposals have to be broad enough and flexible enough to be implemented in very different places with very different structures, priorities, and resources. Personal psychotherapy remains one of the very best routes to psychodynamic sophistication but can no longer be a general requirement of residents, who now enter psychiatry for widely varied motives. A long-term child case is one of the best ways to consolidate the developmental perspective on adult behavior and could be one of the added PGY-3 cases, but it simply cannot be done in many programs. A greater caseload is optimal for achieving certain competence and greater sophistication for all residents, but the goal is no longer to teach all residents how to practice psychoanalytic psychotherapy. The goal is to turn out psychodynamically informed and sophisticated psychiatrists. Given the issue of 3-year versus 4-year programs, we felt that the bulk of the training had to be accomplished after the internship year. And given the widely varied resources and skills available on different services at different programs, we could not insist on a specific structure or specific content. For instance, consultation-liaison services have a strong psychodynamic bent in some programs and almost none at all in others. It was assumed that learning activities at various sites would encourage the application of principles learned while doing individual dynamic therapy to other situations but that the curriculum needed to stand on its own as the primary means of formally teaching these principles.

The task force also considered how a psychotherapy training curriculum could be applied in a program either with limited resources or with such a strong commitment to other areas of psychiatry that few resources are directed to psychotherapy training. Although the model curriculum already represented a distinct compromise of some members' standards, the task force saw the need to establish standards for a minimal training experience as well. In this endeavor, the structural variability of programs again became a concern, so the focus became hours of exposure.

## MODEL CURRICULUM FOR MINIMUM TRAINING IN PSYCHODYNAMIC PSYCHOTHERAPY

This curriculum was designed for training programs that have limited resources to devote to training in psychodynamic psychotherapy. In the opinion of the task force, this curriculum represents the minimum that would meet the new requirements of the Residency Review Committee for Psychiatry. The goal of such a curriculum would be to provide an awareness, knowledge, and appreciation of psychodynamic issues that meet a minimum standard and could be built on through ongoing educational activities. The members believe some knowledge of the unconscious, transference, and therapeutic process is more desirable than ignorance or misunderstanding. The objectives of this curriculum are as follows:

1. To provide an adequate basic background for the general psychiatrist so he or she can later achieve competence as a psychodynamic psychotherapist with additional supervision and training.
2. To provide the general psychiatrist with a beginning language and basic concepts for understanding dyadic interactions and unconscious forces.
3. To provide the general psychiatrist with an awareness of the ongoing and omnipresent role of unconscious forces in all clinical situations.
4. To sensitize the general psychiatrist to the complicated process and evolution of the clinical relationship in all therapeutic settings.

To meet these objectives, each resident must spend a minimum of 200 hours treating patients with psychodynamic psychotherapy. These sessions must be at least weekly and last at least 45 minutes, and the purpose of each session must be to engage in psychodynamic, expressive, exploratory psychotherapy. Preferably, these 200 or more hours of experience will extend over the entire training period of the general psychiatrist. Each resident should see at least four different patients, at least one for more than 50 sessions and at least one, preferably more than one, who is treated until termination; the termination should be planned and dealt with as part of the treatment. A minimum of 100 hours of supervision by well-trained psychodynamic psychiatrists is expected. There must be at least 1 year of weekly didactic seminars on theory and technique and 1 year of weekly case conferences. The readings for the didactic seminars should include at least one widely respected basic text on psychotherapy and one widely respected basic text (or collection of classic papers) on the core concepts of psychodynamic theory.

In addition, there must be an application experience in which the principles learned while practicing psychodynamic psychotherapy are explicitly applied to other settings. This application experience will usually be in the form of a case conference. In the emergency room, emphasis would be on the psychodynamic forces leading to a patient's decompensation at a particular time, family and interpersonal dynamics interfering with a patient's support system, the psychodynamics of suicidal behavior, and the dynamic basis for specific crisis intervention interpretations. In an inpatient setting, the following issues should be covered: the dynamic meaning of psychotic content, family dynamics, psychodynamics of acting out behavior, psychodynamic underpinnings of milieu therapy, psychodynamics of control and authority issues in the doctor-patient relationship, and the definition and psychodynamic basis of "psychosocial support." In a medication clinic, the application conference should deal with the dynamics of compliance and noncompliance, institutional transference, covert positive transference, the unconscious meaning of medication and medication adjustments, and the role of family dynamics in maintenance of stability. On a consultation-liaison rotation, the conference should address the dynamics of the doctor-patient relationship, the unconscious meanings of hospitalization and illness, the adaptive and maladaptive uses of regression, the psychodynamics of grieving and dying, and psychotherapeutic interventions to deal with such issues.

## CONCLUSIONS

The task force had surprisingly little difficulty in finding a shared vision of the psychiatrist of the future. There was a consensus that psychiatrists must continue to be applied psychologists as well as become applied neuroscientists. Further, psychiatrists must be synthesizers and integrators of these fields. This vision is justified from clinical, intellectual, and economic perspectives. Despite the changes in third-party coverage, patients will continue to need and find psychotherapy as best they can, regardless of what system is in place. The task force encountered a large body of anecdotal evidence that young psychiatrists going into practice who integrate psychotherapy into their treatments have more success than those who must refer patients once the hospitalization is over or medication maintenance is achieved.

One major controversy was over whether the model curriculum should be designed so that every psychiatric resident would achieve a full level of competence as a psychodynamic psychotherapist. It was agreed that the curriculum should be thorough enough so that gifted, committed residents could become competent by its completion and that all residents should achieve a level of skill allowing generalization, wide application, and ongoing learning of principles—that is, they should become psychodynamically informed psychiatrists.

The task force gave much attention to the details of the minimum curriculum because it wished to avoid fostering biologically oriented clinicians who are able to offer only an intuitive, unsophisticated form of supportive therapy. It recognized the possibility that the minimum standard might be interpreted as the average expectable standard.

Some might claim that the expressive psychotherapy experience itself is not necessary to produce a psychodynamically informed psychiatrist. These critics might suggest that site-based experiences are sufficient to enable residents to apply psychodynamic principles to supportive therapy, brief therapy, milieu management, etc. What the long-term individual psychotherapy experience uniquely offers is the opportunity to explore, struggle with, and actually use unconscious forces and transference-countertransference interactions in open, explicit ways. It is this process which solidifies both the experiential and the intellectual learning, making the applications more effective, sophisticated, alive, and human.

The task force concluded that the psychiatrist of the future must be deeply and effectively psychodynamically informed and have the opportunity to become psychotherapeutically competent. This can only be done with formal training in expressive, insight-oriented psychoanalytic psychotherapy. This can be accomplished with a carefully planned curriculum spanning 3, or all 4, residency years that will take approximately 13% of training time (based on a 50-hour week). More than this may be desirable but may not be realistic. Less than this may be inevitable in a few settings but is acceptable only if very specific criteria are met.

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# The Biological Basis of an Antidepressant Response to Sleep Deprivation and Relapse: Review and Hypothesis

Joseph C. Wu, M.D., and William E. Bunney, M.D.

*Sixty-one papers involving over 1,700 subjects have documented that over half of depressed patients experience an antidepressant response to sleep deprivation. Eighty-three percent of unmedicated depressed patients who had an antidepressant response to sleep deprivation relapsed after one night of sleep. Short naps can also activate severe relapses. The authors suggest that these phenomenological observations concerning relapse with a night of sleep or with naps after successful sleep deprivation would be compatible with the existence of a sleep-associated depressogenic process.*

(Am J Psychiatry 1990; 147:14–21)

Five efficacious treatments for depression include tricyclic antidepressants, monoamine oxidase inhibitors, ECT, chronic REM deprivation, and psychotherapy. All of these treatments require 1 to 6 weeks to produce an antidepressant response. However, sleep deprivation can produce a dramatic decrease in depressive symptoms within 24 hours. An intensive review of the phenomenology and mechanisms of action of sleep deprivation may provide important clues for understanding the underlying biological substrate of depressive illness and for the future development of rapidly acting antidepressant treatments or drugs. The purpose of this paper is to review the evidence that prolonged wakefulness is antidepressogenic and complementary evidence that sleep is depressogenic in a subgroup of depressed patients. In view of the evidence it is also important to note the well-recognized, apparently paradoxical observations of profound sleep disturbances in depression, including shortened REM latency, decreased delta sleep, and intermittent wakefulness (1) and the observation that pharmacological antidepressants and ECT reverse these sleep disturbances (1).

Schulte (2) was the first to note a possible relationship between sleep loss and the alleviation of depression. He described the case of a teacher who felt better the day after a sleepless night and reported that the less sleep she had the better she felt. This observation inspired Pflug and Tolle (3) to conduct the first therapeutic trials of sleep deprivation as an antidepressant. They noted that the remission was transient and that relapse often recurred on the second day after sleep deprivation. Since these initial studies, other investigators (1, 4) have suggested the possibility that disturbances of sleep may be related to the pathophysiology of depression rather than just being manifested as a symptom of depression.

## ANTIDEPRESSOGENIC AND EUPHOROGENIC EFFECTS OF WAKEFULNESS

### *Sleep Deprivation's Antidepressant Effect*

Figure 1 presents data on a patient who responded to total sleep deprivation and experienced a total relapse in depressive symptoms the day after the following night's sleep. We have reviewed 61 papers published in the last 21 years in 13 different countries and involving over 1,700 individual patients, which have documented that an average of 59% of the patients show a marked decrease in depressive symptoms the day after a night of total sleep deprivation. Sixty-seven percent of those designated as having endogenous depression responded to sleep deprivation; no difference was noted between patients with unipolar and bipolar subtypes of depression. Patients with a diagnosis of neurotic depression had a lower response rate (48%).

Eight of the 61 papers addressed the issue of the timing of the antidepressant response (5–12). Figure 2 shows the mean ratings of the patients in these studies before, during, and after sleep deprivation and after the first night of recovery sleep. Ratings were transformed to match a visual analogue scale. All 34 patients who responded to sleep deprivation are included in this analysis, and the number of independent observations at each time point are indicated in the figure. Only one study (8) reported on the time course of mood changes in patients who did not respond to sleep

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**FIGURE 1. Change in Mood Rating With One Night of Total Sleep Deprivation in a Depressed Patient**

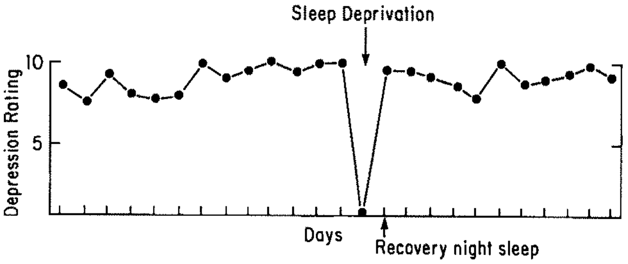
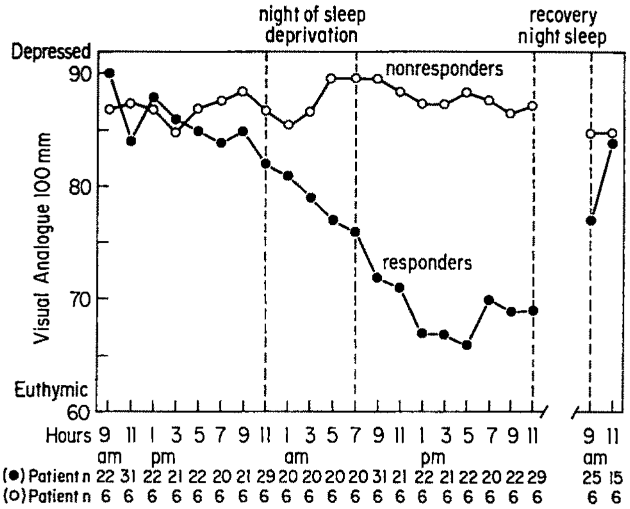


**FIGURE 2. Mean Change in Mood Rating With One Night of Total Sleep Deprivation in Depressed Patients[a]**



[a] Data are from eight sleep studies (5–12), including one study (8) of nonresponders. Studies used self-ratings or observer ratings. The extremes of the analogue scale represent the absolute extremes of the primary instruments. Many of the primary scales were unipolar graphs that ranged from high depression to no depression, with euthymia set at 50% and mania below 50%.

deprivation (figure 2). From figure 2 it can be seen that the average depression ratings of the responders showed a decrease from morning to the evening of the day before sleep deprivation; there was a continuation of this decrease in depression during the night of sleep deprivation and into the next day, and it plateaued between 1:00 p.m. and 5:00 p.m. After a recovery night of sleep there was a relapse in symptoms.

In addition to total wakefulness, which produced a rapid but transient alleviation of depression, Vogel et al. (13) reported that chronic selective awakening of depressed patients from REM sleep without interruption of slow wave sleep produced a gradual but sustained alleviation of depression. Two studies have reported dysphoria related to sleep deprivation in normal subjects (8, 14); however, one of these studies also reported some euphoria in normal individuals (14). Thus, the antidepressant effects of sleep deprivation may be state dependent.

### *Diurnal Mood Changes*

Wakefulness during the daytime may be related to the improvement of mood in some patients with endogenous depression (15). They tend to wake up early in the morning with severe depressive symptoms which progressively decrease during the day so that in the evening they are relatively free from symptoms. The daily decrease in their depressive symptoms may be due to a mechanism similar to that responsible for the decrease in depression that occurs after total sleep deprivation. Some studies have found that subjects who show diurnal mood variation have a better chance of responding to sleep deprivation (11, 16, 17). Relevant to this observation, it is interesting to note that in contrast to the responders in figure 2, the small group of six nonresponders did not show a diurnal decrease in depression ratings during the day before the night of sleep deprivation. Sleep deprivation may act in part by preventing the nocturnal deterioration in mood that often takes place in patients with endogenous depression.

### *Manic Switches After Sleep Deprivation*

Wakefulness or decreased sleep may be euphorogenic as well as antidepressogenic and may be associated with the apparent precipitation of hypomanic or manic symptoms during the day of response to sleep deprivation. Hypomanic symptoms have been reported in 10 studies. An aggregate of patients from these studies (5–8, 16, 18–22) revealed that approximately 30% of the 29 patients with bipolar depression became hypomanic or manic and that 25% of the 84 patients with unspecified depression became hypomanic or manic after a night of total sleep deprivation. Wehr et al. (23) hypothesized that sleep reduction may cause the onset of mania in a number of bipolar patients.

## PROPOSED DEPRESSOGENIC EFFECT OF SLEEP

Since wakefulness may be antidepressogenic, we theorize that sleep is depressogenic. The strongest evidence that sleep is depressogenic comes from studies of relapse following the first night of sleep after improvement. Of the 61 studies reporting sleep deprivation experiments, 17 studies involving 158 responders (see table 1) contained information concerning the timing of relapse in patients who responded to sleep deprivation. Eighty-three percent of patients not receiving medications relapsed after the first night of sleep, compared with only 59% of those receiving medications ($\chi^2=9.82$, df=3, $p<0.01$).

In addition to the previously cited studies, which reported relapse after a recovery night of sleep, four independent investigators have observed that a small subgroup of responders experience relapses after a nap. The first report was in 1979 by Knowles et al. (7),

**TABLE 1. Studies of Improvement in Depression After Partial or Total Sleep Deprivation and Relapse After the First Night of Sleep Following Improvement**

| Study | Depression Subtype | N | Patients Who Responded: Total | Received Medication | Relapsed[a] |
|---|---|---|---|---|---|
| Pflug, 1972 (24) | Endogenous | 12 | 12 | Yes | 1 |
| Voss and Kind, 1974 (25) | Endogenous | 9 | 8 | Yes | 0 |
| Zimanova and Vojtechovsky, 1974 (18) | Endogenous | 20 | 14 | Yes | 11 |
| Cole and Muller, 1976 (20) | Unipolar | 8 | 7 | Yes | |
| | Bipolar | 3 | 1 | Yes | 7 |
| | Unspecified | 4 | 1 | Yes | |
| Loosen et al., 1976 (26) | Unspecified | 8 | 8 | Yes | 0 |
| Pflug, 1976 (5) | Unipolar | 45 | 40 | Yes | 24 |
| | Bipolar | 12 | — | Yes | — |
| | Unspecified | 43 | — | Yes | — |
| | Neurotic | 22 | — | Yes | — |
| Post et al., 1976 (6) | Unspecified | 19 | 10 | No | 9 |
| Sidorowicz, 1976 (27) | Endogenous | 12 | 9 | Yes | |
| | Neurotic | 5 | 2 | Yes | 7 |
| | Unspecified | 2 | 0 | Yes | |
| Philipp, 1978 (28) | Endogenous | 34 | 19 | Yes | 0 |
| Gerner et al., 1979 (8) | Unspecified | 25 | 16 | No | 11 |
| | Normal | 20 | — | — | — |
| Knowles et al., 1979 (7) | Endogenous | 1 | 1 | No | 1 |
| Duncan et al., 1980 (10) | Unspecified | 16 | 9 | No | 9 |
| King et al., 1982 (22) | Bipolar | 3 | 3 | Yes | 7 |
| | Unipolar | 7 | 5 | Yes | |
| Wehr et al., 1982 (21) | Bipolar | 9 | 8 | No | 5 |
| Baxter, 1985 (29) | Unspecified | 22 | 12 | Yes | — |
| | Unipolar | 3 | 3 | No | 3 |
| Nosachev, 1985 (30) | Endogenous | 86 | 65 | Yes | 58 |
| Wehr et al., 1985 (12) | Bipolar | 4 | 4 | No | 4 |
| | Unipolar | 1 | 1 | No | 1 |

[a] Relapses occurred in 115 of 194 patients who received medication and in 43 of 52 patients who did not receive medication.

who completed a longitudinal study of a single individual. The patient showed symptoms of severe depressive mood, loss of interest in normal pursuits, anxiety, memory loss, and preoccupation with thoughts of being penniless. During the sleep deprivation, the patient's depressive ratings dropped significantly. The patient was asked to take a nap at 5:00 a.m. Fifteen minutes of non-REM sleep was documented by EEG. Upon awakening, the patient had a profound relapse with depressive symptoms that persisted for at least 3 hours.

In 1984 Roy-Byrne et al. (31) reported the study of another severely depressed patient. After a night of sleep deprivation, the patient had an almost total remission in depressive symptoms. She was hypomanic, singing and dancing, the day after sleep deprivation. She was then asked to nap at 3:30 p.m. By EEG criteria, there was a 90-second nap of slow wave sleep. The patient then awoke and was so depressed that she accused the staff of giving her a poison. This exacerbation lasted for 2 hours. The patient was then allowed to sleep for 6 hours at her usual bedtime and again awoke with a severe, persistent exacerbation of the depressive symptoms.

Kraft et al. (32) studied seven depressed patients who responded to only one night of total sleep deprivation. One subject experienced a relapse after a 10-minute nap at 3:00 p.m. The type of sleep during the nap was not specified. A fourth study by Wiegand et al. (4) involved a systematic investigation of the effect of naps after improvement in depression with sleep deprivation. They studied 12 patients with 28 episodes of sleep deprivation; 12 sleep deprivation trials produced a positive clinical response. The patients were then asked to take a nap at 1:00 p.m. Six of the 12 patients relapsed after the nap; five had naps with REM sleep, and one had a nap with slow wave sleep only. Of the six who did not relapse, three had naps with just slow wave sleep, and three had naps with REM sleep. The three patients who experienced REM sleep with no relapse had very short REM sleep times of 1 to 1½ minutes. Of the 12 patients studied, those with non-REM sleep had a mean sleep time of 55.5 minutes, whereas those with REM sleep had a mean sleep time of 108 minutes. Thus, REM sleep seemed to be associated with a higher risk of relapse, but it is difficult to dissociate the possibility that a greater amount of total sleep time is relevant. Wiegand et al. (4) have noted that not only do naps cause an acute relapse but those patients who relapse continue to stay depressed through the rest of the day.

Two independent, unpublished studies in our own program further support the observation that relapses in depression can occur after a nap. In the first study, 71% (five of seven) of the depressed patients who responded to sleep deprivation relapsed after a 60-

**TABLE 2. Theories of Antidepressant Effect of Sleep Deprivation**

| Theory | Proponents | Proposed Pathophysiology of Depression | Mechanism of Action of Sleep Deprivation | Mechanism of Action of Relapse With Nap After Antidepressant Effect of Total Sleep Deprivation |
|---|---|---|---|---|
| Sleep-released depressogenic substance | Wu and Bunney | Increased depressogenic substance released during sleep | Blockage of release of depressogenic substance by wakefulness and metabolism or storage of substance during wakefulness | Release of depressogenic substance with onset of sleep |
| Antidepressant substance released during wakefulness | Borbely and Wirz-Justice (33) | Decreased secretion of factor in process S | Greater length of time for S substance to accumulate and reach normal level | Not reviewed |
| Critical time period for production of depressogenic substance | Wehr and Wirz-Justice (34) | Phase advance of sleep-sensitive depression switch into sleep period | Prevention of depression switch activation by wakefulness | Not reviewed |

minute nap. In a second independent study by Reist et al. (personal communication), five of six responding patients (83%) relapsed after a 90-minute nap.

There appears to be a trend toward more relapses with longer naps: Kraft et al. (32), 10-minute naps, relapse in one of seven patients; Wiegand et al. (4), 55-minute naps, relapse in one of four patients; Wu et al. (unpublished data), 60-minute naps, relapses in five of seven patients; Reist et al., 90-minute naps, relapses in five of six patients; and Wiegand et al. (4), 108-minute naps, relapses in five of eight patients. In these studies approximately 50% of the patients who responded to sleep deprivation relapsed after a nap.

## THEORIES OF THE ANTIDEPRESSANT EFFECTS OF SLEEP DEPRIVATION

### *Sleep-Associated Depressogenic Process Theory*

We suggest that the phenomena observed concerning relapse with a night of sleep or a nap after successful sleep deprivation would be compatible with a theory of a sleep-associated depressogenic process. One component of this process might be that sleep could release a substance that is associated with depression and that is metabolized or stored during wakefulness, with a subsequent reduction in depression (see table 2). It should be emphasized that if the suggestion of a depressogenic substance released with sleep is true, this substance is likely to be one of only many factors involved in the complex CNS control of depressive mood. Although we feel that a depressogenic process is most compatible with the observations reviewed earlier, it is certainly possible to hypothesize the existence of a euphorogenic substance that is rapidly metabolized or stored during a night's sleep or a nap and released in wakefulness. In many respects this theory would be similar to the Borbely and Wirz-Justice hypothesis of process S (33).

The hypothesis that depressed subjects are sleep satiated and overaroused has been proposed to account for some of the sleep disturbances seen in depression (1). However, it is also known that depressed subjects are fatigued. Alternatively, a sleep-associated depressogenic process could also influence a regulatory mechanism or marker that measures the amount of sleep a person has had and determines when to stop sleep. (It would be as if a faulty gas gauge read "full" even though the gas tank was actually empty.) If there is an excessive release or activity of this sleep-associated depressogenic process, the patient's sleep might be interrupted by a faulty sleep-satiety marker even if he or she has not received enough sleep. This could account for elements of the sleep disturbance seen in depression. As a patient improves, the excessive release or activity of the sleep-associated depressogenic process could be reduced to normal levels. This normalization would prevent the interruption of sleep. One proposed biological correlate of this regulation of sleep length is increased REM density. Aserinsky (35) observed that in normal subjects who have extended their sleep beyond what is normal, there is a tendency for the duration of successive REM periods to diminish and there is a high degree of REM density from REM period to REM period.

Our theory (see table 2) is supported by evidence that a majority of depressed patients have an antidepressant response to total sleep deprivation. It is also supported by evidence that one night of recovery sleep results in a high percentage of relapse of the antidepressant effect of sleep deprivation.

Our theory can also account for patients with endogenous depression who show a diurnal morning worsening, which becomes alleviated with wakefulness. The predictive nature of diurnal mood swings for the antidepressant effect of sleep deprivation is consistent with our theory. The study by Knowles et al. (7) of a single patient's response to sleep deprivation reported improvement in her mood approximately 20 hours after she awoke, whether that was at 7:00 a.m. or whether that was after her sleep had been shifted so that she woke up at 3:00 p.m. This suggested to Knowles et al. (7) that it was the duration of wakefulness which played a key role in the reduction of depressive symptoms.

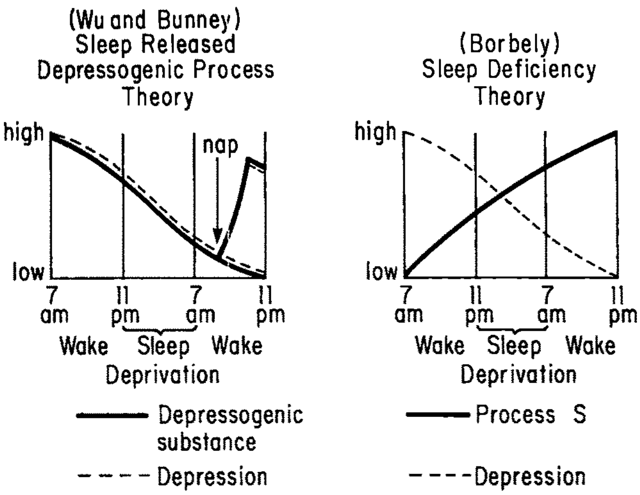
Evidence suggesting the release of a sleep-associated depressogenic substance, as opposed to the release during wakefulness of an antidepressant factor, comes from nap studies. As reviewed earlier, profound depression can recur after naps as short as 90 seconds (32). The rapidity of this phenomenon might suggest the release of a compound during sleep rather than the rapid metabolism of a substance during wakefulness. It is possible that among sleep deprivation responders, there are different degrees of sensitivity to sleep's hypothesized depressogenic characteristics.

Are there examples of sleep-associated processes, models of sleep-associated substances, that are triggered by some mechanism with sleep onset and are reversed during wakefulness? Model substances or systems exist which are activated during sleep and which may be blocked by sleep deprivation. First, it is possible that growth hormone (GH) may serve as a model and fulfill some of these criteria, although it is unlikely to be a depressogenic substance. GH represents a model of a sleep-released substance in man (36). The bulk of GH is secreted during the onset of sleep, primarily in slow wave sleep. GH immediately responds to shifts in sleep schedule and is released at each onset of slow wave sleep (37). However, investigators studying GH release in depressed patients have reported conflicting results; one study (38) showed high GH levels in depressed patients, and others (37, 39) showed low GH levels.

Second, cortisol is another example of a potential substance released during sleep, with the greatest concentration of release coming in the latter half of the night, during which REM sleep is most prominent (37, 39, 40). Some studies have found that sleep deprivation may decrease cortisol secretion (39, 41), whereas others have found no change (42) in normal subjects. Several studies have found evidence suggesting that sleep deprivation reverses dexamethasone nonsuppression in depressed patients, and reduction in cortisol secretion by sleep deprivation appears to be associated with a favorable mood response (43, 44).

If REM sleep during naps is associated with the onset of depression in some patients, as suggested by the work of Wiegand et al. (4), then biochemical REM-related events might offer a third model. Relapse, after REM sleep, of the antidepressant effect of sleep deprivation might be due to increased cholinergic firing and low catecholaminergic and serotonergic tone (45). This would be consistent with the adrenergic and cholinergic theory of depression (44, 46) and with the supersensitive cholinergic theory of depression (which hypothesizes an enhancement of cholinergic activity during depression) (47). However, this theory would not account for the relapses seen after naps with just slow wave sleep (4, 7, 31).

**FIGURE 3. Schematic Diagrams of Two Proposed Models of Sleep Deprivation**[a]



[a] Wu and Bunney's model proposes a mechanism of a hypothetical sleep-released depressogenic substance that is metabolized with wakefulness, and Borbely and Wirz-Justice's model (33) proposes a hypothetical sleepiness process that increases with wakefulness and has euphorogenic properties.

### *Process S Theory*

Borbely and Wirz-Justice (33) have hypothesized that the regulation of the sleep/wake cycle is determined by two factors: a circadian propensity for sleep, process C, and a sleepiness process, process S, that accumulates with increasing time since the last period of sleep (see table 2). Process S is hypothesized to accumulate more slowly in depression (figure 3). This hypothetical process S could play a signal role, providing information to the brain on how long it has been since the organism has last slept. When the duration is long enough, there is an increasing propensity for the activation of sleep-induction programs in the brain (33, 48). Borbely and Wirz-Justice have hypothesized that when process S is low, patients are depressed; and when process S is high (as would happen with prolonged wakefulness), patients are euthymic (see table 2 and figure 3).

Thyroid-stimulating hormone (TSH) is one compound that might provide a model of an endogenous compound that is released with prolonged wakefulness. Parker et al. (49) noted that TSH release appears to be mediated by two factors. First, there is a circadian propensity for the release of TSH beginning in the early evening. The second factor that appears to curtail continued release of TSH is sleep onset. Baumgartner and Meinhold (50) noted that TSH was released during sleep deprivation and that clinical improvement was correlated with change in TSH. Wehr and Sack (51) have proposed that TSH release might be inhibited in depressed patients because they have a higher core body temperature. They suggested that sleep deprivation might act through enhancing radiant heat loss. Figure 3 contrasts the depressogenic process theory to the process S theory.

### *Internal Coincidence Theory*

A third hypothesis focuses on the timing of wakefulness rather than the duration of wakefulness (see table 2). Wehr and Wirz-Justice (34) have proposed the existence of a depression switch occurring in the early morning, which is activated when the switch is advanced from its normal position during the waking hours to the early morning sleeping period. Sleep deprivation prevents the depressive switch from being reactivated by sleep.

Evidence for the sleep-sensitive depression switch, as proposed by Wehr and Wirz-Justice, comes from several studies. Wehr et al. (52) found that shifting sleep forward by 6 hours, from the usual 11:00 p.m.–7:00 a.m. to 5:00 p.m.–1:00 a.m., resulted in complete remission for two of six patients with bipolar depression and partial remission for two more patients. This suggested the possibility that it is the timing, not the duration, of sleep that determines sleep's depressogenic character. Partial sleep deprivation during the second half of the night has also been shown to be effective in causing a remission of depression in some patients (48, 53–55) but not in others (7). Surridge-David et al. (56) reported that a 6-hour phase delay of sleep in 10 young male subjects resulted in two subjects becoming noticeably depressed.

Wehr and Sack (51) noted that there may be an apparent phase advance of the timing of REM sleep in depressed subjects; since there is a shortened REM latency and the majority of REM sleep occurs at an earlier time. Other measures such as 3-methoxy-4-hydroxyphenylglycol, temperature, and cortisol rhythms may also be phase advanced in depressed subjects. This phase advance is consistent with the possibility of a vulnerable depression switch, which is moved into the sleep time of the early morning.

Knowles et al. (7) have presented data from one patient that might be inconsistent with the critical phase hypothesis. Although the depressed subject studied by Knowles et al. (7) responded with a remission of depressive symptoms after total sleep deprivation, there was no alleviation of these symptoms when the subject was either awakened by the experimenters or spontaneously awoke during the latter half of the night, during the hypothesized sleep-sensitive depression time. The mood of the depressed subject lifted 20 hours after the period of last sleep, whether that time was at 2:00 p.m. or 3:00 a.m. Naps have also been shown to result in a relapse of the antidepressant effect at periods of time later than the proposed sleep-sensitive switch time.

## METHODOLOGICAL ISSUES AND FUTURE INVESTIGATIONS

There are important methodological problems in the sleep deprivation literature. None of the 61 studies used a double-blind, placebo-controlled design because of the difficulty in ensuring that the subjects and the experimenters are blind to a manipulation such as sleep deprivation and in part because of the difficulty of finding a suitable placebo control. It is possible that the antidepressant response could be due to experimental bias expectations or the nonspecific effects of attention by the raters. However, the study of Gerner et al. (8) did use normal control subjects who were subjected to sleep deprivation, just as were the depressed patients. Gerner et al. (8) found that normal control subjects did not show a euphorogenic effect with sleep deprivation. Gerner et al. (8) and Post et al. (6) informed subjects and raters that the purpose of the sleep deprivation was to assess changes in biochemistry. Mood effects were presented as incidental to the study. Despite this, both studies reported significant antidepressant effects. Pflug and Tolle (3) used a single-blind design by informing patients that the purpose of sleep deprivation was to assess change in opthalmodynamometry and also found significant antidepressant effects.

There are several lines of evidence that need to be considered in a balanced evaluation. First, not all depressed patients respond to sleep deprivation or circadian manipulation. Thirty-six percent of patients with endogenous depression showed no antidepressant response to sleep deprivation. Furthermore, not all patients who do respond show a subsequent relapse after one night of sleep. Approximately 12% of unmedicated responders show a persistent antidepressant response after a recovery night of sleep. It may be that there are different subtypes or phases of depression that vary in sensitivity to sleep manipulations.

There are methodological issues to be considered in future investigations of the depressogenic sleep theory. There need to be further replications of the phenomenology of the relapse associated with sleep and the antidepressogenic aspects of wakefulness.

Sleep deprivation and nap studies offer a unique opportunity for investigators to experimentally determine the time of day for change from euthymia to profound depression and an opportunity to collect systematic psychobiological data before and after the mood change. It would be important to identify which variables distinguish subgroups of depressed patients who respond to sleep deprivation. Additional nap studies after total sleep deprivation, with sleep EEG monitoring, would help clarify whether slow wave sleep or REM sleep is more important for the relapse. If REM is more important, aminergic and cholinergic mechanisms would be supported; whereas, if slow wave sleep is more important, then the proposed process S will be supported. The time of the nap during the day and the duration of the nap may be important variables requiring control. The use of frequent mood ratings is also important to study the duration of wakefulness required for the antidepressant change and the timing of the relapse. It is not yet clear whether the antidepressant change occurs in response to total duration of sleeplessness, as suggested by Knowles et al. (7), or as a result of the deprivation of sleep at a particular time, as suggested by Wehr and Wirz-Justice (34). Similar questions about the timing of the relapse can be raised. The findings of Southmayd et al. (57) suggest that there is a critical period in the early morning when relapses occur. However, other nap studies at times other than the early morning have noted relapses after the nap.

If there is a depressogenic substance released with sleep, it might be possible to develop a bioassay to isolate and eventually characterize this substance, although at the present time no information exists concerning its possible structure. The pharmaceutical industry certainly has developed the capability of developing long-term analogues for identified compounds, which can serve as competitive inhibitors of such a hypothesized substance. Other possible mechanisms for the mood elevation of sleep deprivation that should be explored include down regulation of serotonin or beta receptors (58). These phenomena have been found with most other effective antidepressant interventions (59). Alternatively, it has been reported that sleep deprivation may increase homovanillic acid, a possible index of presynaptic dopamine turnover (8). The use of modern brain imaging techniques might shed further light on sleep deprivation. We have developed recent preliminary evidence that sleep deprivation may be associated with change in F-18 deoxyglucose utilization in the caudate (60). This finding needs further investigation.

The potential for implementing synergistic treatment combinations for depression needs to be explored. As reviewed earlier, the relapse rate, after one night of recovery sleep, of patients who are taking tricyclic antidepressants and who have had a positive response to sleep deprivation is significantly lower than that of patients who are drug free. Baxter reported that the relapse is prevented in some patients with a positive response to total sleep deprivation if they are taking lithium (29). Pharmacological treatments for depression might be effective in part by inhibiting the hypothesized depressogenic substance.

## SUMMARY

In summary, we have reviewed the evidence that sleep might be depressogenic and that wakefulness might actively counteract this property of sleep in some depressed patients. The 24-hour efficacy of sleep deprivation is more thoroughly established than is generally appreciated. Patients who are taking medication have a significantly lower tendency to relapse after a recovery night's sleep than do patients who are not taking medication. A significant number of patients who respond to sleep deprivation experience hypomanic symptoms during the day after sleep deprivation. Periods of sleep during the recovery night and naps at various times during the day after successful sleep deprivation can reactivate severe depressive symptoms. In some patients, it appears as if REM sleep may increase the relapse rate, although some patients relapse after slow wave sleep. We propose the hypothesis that this modulation of emotion by the sleep/wake cycle might be mediated by a depressogenic process, and possibly in part by a substance that is released during sleep and metabolized during wakefulness.

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# Differential Diagnosis and Classification of Apathy

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*This paper discusses the definition of apathy, reviews its differential diagnosis, and proposes a classification for the conditions that may produce it. Apathy is defined as diminished motivation not attributable to diminished level of consciousness, cognitive impairment, or emotional distress. In its differential diagnosis, abulia, akinesia and akinetic mutism, depression, dementia, delirium, despair, and demoralization must be ruled out. Classification of apathy is organized in terms of its adaptive and functional consequences, its relationship to personality or to sociocultural or environmental events, and its association with psychiatric, neurological, and medical disorders. An approach to assessment and treatment is proposed.*

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Apathy is a familiar and salient feature of many psychiatric, neurological, and medical diagnoses. In addition, it has broader relevance to human functioning, which is evident in its occurrence in response to personal tragedy, natural catastrophe, social loss, environmental deprivation, and role change. Conceptually, apathy is closely linked to motivation and emotion. Perhaps because this conceptual significance has been rarely noted, little attention has been given to the theoretical or clinical aspects of apathy (1). Alternatively, the clinical utility of apathy may not have been considered previously because of difficulties in distinguishing it from other syndromes, such as depression, despair, and abulia. In the absence of a clear definition, it is understandable that apathy has not been the object of systematic investigation. This paper, which is part of an ongoing project evaluating the validity of a scale for the measurement of apathy (R.S. Marin, R. Biedrzycki, and S. Firinciogullari, unpublished manuscript, 1989), describes the differential diagnosis and classification of apathy and presents an approach to its evaluation and treatment based on this classification. The material is intended primarily for clinicians. However, many research questions are raised by the study of apathy; some of these are highlighted in the concluding section.

## DEFINITION AND DIFFERENTIAL DIAGNOSIS

Apathy, which is derived from the Greek *pathos*, or passions, is defined conventionally as absence or lack of feeling, emotions, interest, or concern. This definition is helpful for general purposes but has weaknesses when one is dealing with some of the common clinical disorders associated with apathy. For example, patients with frontal lobe injury may seem apathetic because they lack interest or motivation, but the fact that they may also be violent, irritable, or euphoric does not seem consistent with the notion that apathy denotes lack of emotion. Similarly, depressed patients may be described as apathetic, despite the fact that they are in great emotional pain rather than lacking in emotional expression. How can we define apathy for clinical purposes so as to account for these inconsistencies?

I suggest approaching the definition of apathy in the same way that we try to define other clinical terms. If we consider its clinical applications, it will be seen that apathy does indeed refer primarily to lack of motivation. Depressed patients *are* called apathetic because they profess loss of motivation. Similarly, frontal lobe syndromes are characterized by lack of interest or involvement in usual activities. However, if we simply define apathy as a state of diminished motivation, we confront the fact that it is but one of a number of amotivational states encountered in clinical practice. How, then, does the presence or absence of emotion enter into the definition of apathy? In the same way that we call patients aphasic only if their language is not disordered by an impairment of consciousness, attention, or general intellectual activity (2), apathy describes only those patients whose lack of motivation is not attributable to a diminished level of consciousness, an intellectual deficit, or emotional distress. Apathy is, therefore, a state of primary motivational impairment. For clinical purposes, individuals who show such primary motivational impairment may be regarded as having apathy syndromes (see appendix 1). Frontal lobe injuries are included among the states that may produce apathy syndromes because the lack of motivation of patients with these conditions is not attributable to emotional distress. In other instances, lack of motivation is a consequence of other problems (e.g., dysphoria) and is best regarded as a feature

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or symptom of the syndrome in question (e.g., depression). It is these syndromes—delirium, dementia, depression, abulia, akinesia and akinetic mutism, and despair and demoralization—that constitute the differential diagnosis of apathy.

*Delirium* is a transient state of disordered consciousness in which patients show 1) impaired capacity to shift or maintain attention, 2) fluctuating levels of consciousness, 3) memory disturbance, 4) perceptual disturbances, 5) a variety of affective symptoms, including blunting or flattening of affect, and 6) behavioral changes, including agitation, withdrawal, and lack of interest. When lack of interest in the environment, lack of goal-directed behavior, and flat affect predominate, delirium resembles apathy. Lethargy, anergy, and drowsiness, which are seen in some delirious patients, are other features of delirium that may suggest apathy.

*Dementia* is an acquired syndrome of intellectual impairment sufficiently severe that social or occupational functioning is impaired (*DSM-III*). Patients with dementia often become apathetic, although the mechanisms of this apathy have not been studied. Recent evidence (3) suggests that in Alzheimer's disease, apathy tends to occur in the confusional stage of the disease. This apathy has been attributed to loss of the cognitive capacities needed to organize goal-directed behavior (3). However, psychological factors (e.g., perception of diminished capacities) and neurological factors (e.g., involvement of specific limbic brain regions, such as the frontal lobe, amygdala, and cingulate gyrus) provide other explanations. Similarly, in multi-infarct dementia, there are multiple possible psychosocial and neurological mechanisms for apathy (e.g., the location of infarction in a particular patient) (see the section on organic disorders later in this paper).

*Depression* is another syndrome in which apathy may appear. Many studies (1, 4–7) have documented the occurrence of apathy in depression, and, in fact, clinicians often regard depression as a model disorder for defining apathy. This is misleading, however, because there are a number of ways in which the apathy of depression, or what one might call depressive apathy, is distinguishable from other disorders (e.g., frontal lobe syndromes) in which apathy occurs as a syndrome per se. The description of depressed patients as apathetic is based on their inactivity, such as social inactivity, and their claims that they have lost interest in their usual activities. Paradoxically, there are a variety of ways in which depressed patients show features that are inconsistent with apathy. In comparison to apathetic patients, who are passive or compliant, depressed patients are generally quite deliberate and active in their avoidant behavior. For example, they may staunchly resist attempts to involve them in treatment or normal socialization. In the extreme, depressed patients are suicidal, which, clearly, does not reflect apathy but negativism and despair. This negativism is generally clearest in the thought content of depressed patients, who characteristically emphasize pessimism and hopelessness, often in association with self-deprecatory thoughts. These latter features contribute to the dysphoric affect that is virtually a sine qua non of depression and definitively distinguishes depression from true apathy, in which, by definition, one expects a lack of emotional distress.

*Abulia*, which is derived from the Greek *boul*, or will, is usually defined as a lack of will or motivation or an inability to decide. In clinical practice, the diagnosis is reserved for patients who are awake but otherwise severely impaired in their ability to communicate and to initiate and self-regulate purposeful behavior. Therefore, from a conceptual standpoint, abulia and apathy are on a continuum of motivational and emotional deficit, abulia representing the more severe portion of the continuum. This relationship is borne out by the fact that neurological dysfunction which causes apathy tends to produce abulia when the dysfunction is more severe, as in frontal lobe tumors.

*Akinesia* is usually defined as a disorder of movement, in contrast to apathy, which denotes loss of motivation. Akinetic patients show diminution or loss in the initiation of movement. In clinical practice the term is reserved for patients in whom the lack of movement is not attributable to elementary motor deficits, such as hemiplegia, or psychiatric states, such as catatonia. Thus, akinesia is primarily a motor disorder, usually attributed to basal ganglia dysfunction, and tends to be associated with other motor disturbances, including bradykinesia, rigidity, and abnormal movements such as tremor, chorea, and athetosis. It is of interest, however, that in practice akinesia often occurs with apathy; in fact, Rifkin et al. (8) have suggested that akinesia be considered a disorder of behavior in which apathy is a prominent feature (see the section on drugs and medical disorders later in this paper).

*Despair and demoralization* are psychological states occurring primarily in normal individuals in response to the experience of overwhelming stress (9). This may be contrasted to the previously discussed states, which refer to individuals who are ill. Both despair and demoralization share with apathy a loss of motivation. They differ from apathy, however, in that apathy denotes, as well, a lack of concern or emotional distress, whereas despair and demoralization are experienced as dysphoric, unpleasant states. In other words, it would be illogical to say that someone is *suffering* from apathy, whereas despair and demoralization are experientially painful psychological states. In addition, the concepts of despair and demoralization must be understood in terms of an individual's affective orientation to the future. In principle, apathy carries little or no connotation in this regard, whereas those suffering despair or demoralization express a loss of hopefulness or meaningfulness with respect to the future.

## CLASSIFICATION

As suggested by the foregoing review of apathy's differential diagnosis, apathy may be caused by diverse circumstances arising as part of normal development or human experience as well as from a variety of medical, psychiatric, and neurological conditions. The following classification organizes the causes of apathy into three major areas on the basis of the answers to three questions.

### *Is Apathy a Characteristic or an Acquired Feature of Adult Personality?*

It is common knowledge that among apparently normal individuals, there are some who are relatively apathetic and others who are highly motivated. Among individuals in whom apathy is characteristic of adult personality, there are some in whom the apathy is restricted to specific areas of psychosocial functioning and others in whom it is a pervasive characteristic. Those for whom the apathy is severe or pervasive enough to interfere with psychosocial functioning would meet the *DSM-III* criteria for personality disorder. For example, Neugarten et al. (10) described older adults with an apathetic pattern of normal aging characterized by lifelong characteristics of passivity, low role activity, low self-esteem, and low life satisfaction. A more common relationship to personality disorder is seen in those instances in which apathy is secondary to a recognized personality disorder, such as avoidant or schizoid personality, in which individuals seem uninterested or uninvolved because of their fears or inhibitions.

In contrast to the adaptive problems associated with pervasive apathy, it is common for normal individuals to be apathetic about some things. Thus, the apathy seen in normal individuals occurs in the context of an overall state of being normally concerned or motivated in many areas of psychosocial functioning. For this reason, apathy that is consistent with and characteristic of normal functioning may be called selective or relative apathy. Selective apathy is adaptive, and in most instances it simply reflects the fact that a person has not acquired or maintained interest in a particular activity. Selective apathy may serve defensive purposes as well (11). Last, one might view eccentric individuals who are interested in a narrow range of activity as showing an extreme form of selective apathy, although such restriction of range should not be viewed as characteristic of eccentric persons in general (12).

### *Does Apathy Represent a Response to Diminution in the Perceived Rewards or Incentives of the Person's Environment?*

If apathy represents an acquired feature of adult personality, the first question to ask in classifying it further is whether it has developed in association with a decrease in available rewards or incentives. This category of apathy takes into account many otherwise diverse factors that disrupt normal emotional and motivational functioning. For clinical purposes it is useful to subdivide such factors into two groups: socioenvironmental and biological.

*Socioenvironmental factors.* Major changes in the social or physical environment may impair motivation by removing usual or expectable sources of reward or incentives. The loss of motivation and emotional responsiveness sometimes associated with institutionalization (e.g., in prisons, nursing homes, or chronic psychiatric facilities) is an example familiar to psychiatrists. When cultural or language differences interfere with the pursuit of values or goals (e.g., among immigrants or minorities segregated from the ambient and dominant culture), one sees a variety of motivational and emotional adaptations, of which apathy is one. Natural calamities such as floods, earthquakes, and tornadoes profoundly disrupt normal motivation, producing states of "psychic numbing" characterized by "apathy, withdrawal, depression and overall constriction in living" (13). In survivors of the Holocaust and the atom bomb attacks on Hiroshima and Nagasaki, similar reactions have been described (9).

In less severe cases of social disturbance, such as the loss of role function associated with retirement, the conclusion of child-rearing responsibilities for a homemaker, or other phase-of-life transitions, people commonly describe a purposelessness or lack of direction in the absence of emotional distress, that is, apathy. Elderly people may be particularly at risk for apathy arising from such psychosocial sources. In fact, some older individuals are influenced by the culturally derived but internalized expectations that one *should* become withdrawn or apathetic in later life (10). Simultaneously, the older person's social environment may no longer provide vocational, social, or financial opportunities for continued engagement in the activities that had defined optimal motivational functioning. Change of residence and, in particular, institutionalization are relatively extreme examples of environmental changes that may produce apathy in this way.

*Biological factors.* A variety of biological events, such as loss of peripheral sensory or musculoskeletal capacities, may produce diminution in the perception that there are sufficient rewards and incentives available in the environment to sustain behavior. (Central neurological dysfunction is discussed in the next section.) In elderly persons especially, loss of hearing and of visual ability may produce an insidious decrease in motivation. Misjudging the associated dysfunction as due to depression or early dementia may lead to errors in treatment or prognosis. Loss of motor effector systems, as in traumatic paraplegia, may produce apathy by essentially the same psychological mechanism.

### *Is Apathy a Feature of Some Identifiable Psychiatric, Neurological, or Medical Disorder?*

*Psychotic and affective disorders.* The conceptual relationship of apathy to depression has already been discussed. The association of apathy with adult depressive disorders has been documented in multiple factor analytic studies of patients with depression (1, 4–7). Spitz's description of anaclitic depression in infants

(14) included a stage of withdrawal and diminished responsiveness to the environment. Apathy is also frequent in adolescent depression (15). In comparison to younger adults, elderly depressed patients are less likely to show depressed mood, whereas they more frequently show apathy, anergy, pessimism, somatic complaints, and cognitive dysfunction (16). Illustrating the complexity and importance of differentiating the causes of apathy in the elderly is the following comment of Raskin and Sathananthan (17): "One has to be careful to separate out the apathy and withdrawal that is often seen in aged persons from the apathy specific to depression in this age group. One also needs to distinguish the apathy seen in depressed elderly from the motor retardation and emotional withdrawal that occurs in other psychiatric conditions such as schizophrenia."

An extensive literature addresses the changes in emotional and motivational state accompanying chronic schizophrenia. A variety of terms have been used to describe the same phenomena, including "changes in affectivity" (18), "flat affect" (19), "amotivational syndrome" (20), "emotional blunting" (21), "negative symptoms" (22), and "type II schizophrenia" (23). Apathy in schizophrenia is of particular interest because it is a recognized clinical state that is not simply a symptom of some other clinical syndrome but, instead, strongly characterizes the clinical picture. This is evident in the following vivid portrait written by Bleuler (18): "Many schizophrenics . . . sit about the institutions to which they are confined with expressionless faces, hunched up, the image of indifference. They permit themselves to be dressed and undressed like automatons, to be led from their customary place of inactivity to the messhall, and back again without expressing any sign of satisfaction or dissatisfaction. They do not even seem to react to injuries inflicted on them by other patients" (p. 40).

Currently, these characteristics of schizophrenia are receiving renewed interest (22–25). Their clinical importance was underscored by Ullman and Krasner (26), who stated that "apathy" or "lack of interest in the environment . . . [is] . . . probably the major treatment problem when working with chronic schizophrenic patients" (p. 400).

Postpsychotic depression refers to a depression occurring in the wake of a period of schizophrenic or other psychotic disorder. Although the term implies similarity to depressive disorders, it is questionable whether the phenomenology of the disorder always justifies the comparison. Some reports (27) have documented elevated depression ratings in patients with postpsychotic depression. However, Floru et al. (28) stated that the condition is "seldom expressed by genuine deep melancholy or depressive contents but by apathy." Other terms used to describe patients with postpsychotic depression, including "lack of vital impulse," "lack of desire" (28), "wooden" demeanor (29), lack of initiative (30), and paucity of spontaneous speech (31), also suggest a similarity to apathy rather than to depression. These observations suggest that in some patients, postpsychotic depression is more accurately described as a syndrome of apathy than of depression. The inconsistencies in the literature may have to do with the fact that depression scales do not permit discrimination of depression and apathy when scores are given as total scores. For example, a patient who is primarily apathetic might endorse items for decreased energy, interest, libido, and psychomotor speed and not endorse items specific to depression, such as depressed mood, guilt, suicidal ideation, and sleep disturbance.

*Organic disorders.* As indicated, both delirium and dementia may produce apathy. Delirious patients who are agitated and emotionally aroused are usually not considered apathetic. Apathy is more likely to be thought present in cases of delirium characterized by drowsiness, sedation, or hypoactivity. In such hypoaroused delirious states, the sedation results in failure to initiate behavior. The mechanism may be interference with the ascending reticular activating system by medical illness (e.g., renal or hepatic failure), by drugs (e.g., sedative-hypnotics), or by a structural lesion (e.g., a brain tumor or subdural hematoma) that compromises these critical brainstem regions. Given the large number of agents and conditions that may produce toxic-metabolic encephalopathies (32), it is clear that numerous medical illnesses need to be considered in the etiological evaluation of patients with apathy.

Dementia and organic amnestic disorders are two other syndromes of cognitive impairment that have been associated with apathy. The production of apathy by Alzheimer's disease was mentioned in the discussion of differential diagnosis. Several causes of dementia involving primarily basal ganglia pathology have been referred to collectively as "subcortical dementias," in part on the basis of similarities in several of their neuropsychiatric features, including forgetfulness, slowness of thought processes, impaired problem-solving capacities, and, finally, personality change in which apathy, depression, euphoria, or irritability may occur (33). The term "subcortical dementia" encompasses Parkinson's disease, Huntington's disease, and progressive supranuclear palsy. Marsden and Parkes (34) stated that in some Parkinson's disease patients, one sees "blunting of interest and drive, amounting to apathy, a limitation in intellectual activity, and an apparent slowing of thought process and memory." In their review of the literature on progressive supranuclear palsy, Albert et al. (35) found that apathy and depression were more common personality disturbances than irritability and euphoria. Caine et al. (36) observed that in Huntington's disease patients, apathy arises primarily from lack of initiative, not lack of affect or persistence. The coexistence of apathy with subcortical pathology and cognitive impairment is also seen in patients with multiple vascular insults to paramedian diencephalic structures (37).

With regard to organic amnestic disorders, it is of interest that for Korsakoff's syndrome, which is generally characterized in terms of the amnesia that accompanies it, there is a lengthy literature emphasizing loss of motivation (38). It should be noted that the pathology of Korsakoff's syndrome primarily involves diencephalic structures, particularly the mammillary bodies and medial dorsal thalamus. Korsakoff patients generally have the capacity for normal emotional display, but their initiative and emotional response to important events are decreased.

A separate group of apathetic patients are those demented individuals in whom there is profound loss of behavioral, cognitive, and emotional capacities, producing states of mutism or abulia. Akinetic mutism refers to a syndrome in which there is virtual absence of movement and communication by patients who are fully awake and do not have paralysis (39). The syndrome occurs as a result of bilateral damage to one or more of the following areas: cingulate gyri, septal region, frontal poles, thalamus, or hypothalamus (39). In cases of unilateral cingulate involvement, the diminution in the capacity to express and experience emotion is less severe, producing an apathetic, rather than an abulic, state. Damasio and Van Hoesen (40) described a patient who suffered infarction involving the cingulate gyrus, supplementary motor area, and mesial motor area. In addition to weakness of the contralateral lower extremity, the patient showed what "could best be described as akinesia and mutism, but might as well be designated as a state of aspontaneity and nonlateralized neglect of most stimuli," since she reported that prior to recovery she had had " 'nothing to say.' Her mind was 'empty.' 'Nothing mattered.' She apparently was able to follow our conversations even during the early period of illness, but felt no 'will' to reply to our questions. In the period after discharge she continued to note a feeling of tranquility and relative lack of concern."

There are many reports in the literature which document the fact that patients with right hemisphere stroke may develop what was originally called by Babinski (41) the indifference reaction. Babinski and more recent workers (42–44) have variously described such patients as showing lack of emotional concern, lack of emotional expression, inappropriate cheerfulness, or apathy. Robinson et al. (44) found apathy more associated with lesions in the anterior part of the right hemisphere. Other personality changes in such patients include irritability and angry outbursts. Confirming the motivational significance of the indifference reaction are reports of slower recovery of social and motoric function in patients with right, as compared to left, hemisphere damage (45).

Destructive neurological lesions that affect the amygdala and anterior temporal lobes bilaterally may produce a syndrome of "blunted affect, apathy, and pet-like compliance" (46). Such patients are thought to represent human cases of the Kluver-Bucy syndrome, originally described in monkeys who had undergone bilateral temporal lobectomy (47). Human cases of the Kluver-Bucy syndrome have been caused by almost every category of neurological disorder, including trauma, surgery, tumor, vascular lesions, and degenerative diseases.

Finally, mention should be made of what is perhaps the best-known cause of apathy arising from neurological damage, the so-called frontal lobe syndromes. The complex clinical picture presented by patients with these syndromes and our developing, albeit limited, understanding of the neurobehavioral relationships seen in such patients suggest that the term itself is too general (48). Blumer and Benson (49) distinguished among frontal lobe patients according to the region of the frontal lobes involved. They suggested that "slowness, indifference and apathy" may predominate in patients with convexity lesions, whereas loss of social graces, impulsive anger, violence, inappropriate sexual behavior, and inappropriate wit are more typical of patients with orbitofrontal lesions. Nevertheless, it has been frequently reported that victims of frontal lobe brain damage show an impairment in initiating and carrying out behavioral tasks. A general lack of concern and interest accompanies these behavioral changes, while affective alterations in the direction of superficiality and impulsivity are commonly seen. Euphoria, silliness, or inappropriate anger and, occasionally, rage occur (40, 48, 50). Even patients who show such marked emotional expressions frequently show "an underlying background of abulia and apathy" (50).

*Drugs and medical disorders.* The discussion of delirium highlighted the fact that there are numerous medical conditions which may produce apathy as a component of delirium. It is also well-known that elderly patients who develop hyperthyroidism sometimes appear apathetic, which is a paradoxical presentation in view of the hypermetabolic state produced by thyroid hyperactivity (51). Bachman and Albert (52) reviewed evidence that hypoparathyroidism and pseudohypoparathyroidism may present with behavioral abnormalities similar to those seen in individuals with frontal lobe injuries, an especially interesting similarity in view of other evidence suggesting that the features of both conditions may be mediated by abnormalities of central dopaminergic systems (52).

Drugs of several sorts may be responsible for apathetic states. Perhaps best-known is the reported association of chronic marijuana use with an amotivational syndrome (53), although the question of whether the apathy of these individuals represents a physiological or a psychosocial consequence of marijuana abuse has not been resolved. The occurrence of apathy in association with neuroleptic drugs is of particular interest. Akinesia, which is generally defined as a disorder of movement, has been shown to include prominent changes in affect, including apathy (8). In fact, Rifkin et al. (8) defined akinesia as a "behavioral state of diminished spontaneity characterized by few gestures, unspontaneous speech, and, particularly, apathy and difficulty with initiating usual activities." Their report suggested that patients who take antipsychotic drugs are frequently at risk for apathy occurring in association with the motor changes which usually define akinesia. Apathetic states also occur in the wake of cocaine or amphetamine discontinuation by chronic abusers. In cocaine addicts (54) these symptoms include anergy, depression, decreased sexual interest, and psychomotor retardation. Some of their symptoms (e.g., hypersomnia, hyperphagia, and decreased concentration), however, are not part of an amotivational picture per se.

## ASSESSMENT

The following guidelines for assessment of apathy are based on the foregoing discussion of the differential diagnosis and classification of the syndrome. A careful psychosocial history, incorporating information from family members, if possible, is needed in order to evaluate whether apathy has been present throughout adult life or whether it represents a change in personality. For those in whom apathy is a feature of adult personality, it is important to ascertain whether the apathy is deviant or normative for the individual's society or subculture. The evaluation of personality and sociocultural environment will also clarify whether the apathy is a pervasive feature of personality or whether it is selective. Identification of individuals' skills, accomplishments, and social relationships will distinguish between persons in whom apathy is adaptive and selective and those in whom it is defensive or pervasive.

When apathy is an acquired feature of adult personality, it is important to evaluate the possible contributions of multiple socioenvironmental and biomedical factors. Natural or personal catastrophes can usually be identified easily. Less severe stressors, such as retirement, change of residence, loss of a job, divorce, and role change, also produce diminution in motivation. Loss of motor capacities is usually identified easily by history and physical examination. However, cognitive impairment and sensory loss may develop insidiously. In this situation, patients' perceptions of environmental reward or incentives may change with little or no awareness on their part. Thus, evaluation for mild degrees of sensory or cognitive loss is important in such patients. Elderly persons are at higher risk for apathy because of the prevalence of many of these psychological, sociocultural, and biomedical causes of apathy in their lives.

With respect to the psychiatric, neurological, and medical conditions that enter into the differential diagnosis of apathy, a comprehensive psychiatric and neuromedical assessment is called for. It is important to look for a history of psychosis in order to determine whether apathy represents residual or negative symptoms of schizophrenia. In such cases the apathy is likely to have been long-standing. A recent episode of psychosis may be a clue to postpsychotic depression, in which apathy may be prominent. Recent psychosis may also be a clue to psychotomimetic abuse. Finally, psychosis may also be linked to apathy because psychotic patients often receive neuroleptics, which may produce akinesia and apathy.

In general, apathy resulting from depression is diagnosed by the fact that the patient is, paradoxically, not truly apathetic. With some exceptions, depression is a dysphoric state, so that depressed patients who claim to be uninterested or unmotivated will also report low self-esteem, self-deprecatory thoughts, anxiety, depressed mood, hopelessness, etc. Also, they are likely to have vegetative signs of depression. On the other hand, depression in the elderly is sometimes distinguished by apathy in the absence of emotional disturbance and depressive thought content. Previous history of depression, thoughts of futility or hopelessness, somatization, and other physiological changes of depression may help in establishing the diagnosis in these cases.

A complete neuromedical evaluation will lead to a clarification of multiple possible etiological factors. Evaluation of thyroid function is, of course, pertinent in evaluating apathetic patients for the possibility of "apathetic" hyperthyroidism (51). Delirium which may be produced by numerous toxic or medical disorders, may produce apathy. Therefore, the evaluation of patients with apathy may require consideration of a large number of toxic-metabolic conditions (12). The presence of elementary sensorimotor abnormalities is helpful in clarifying this differential diagnosis. In the elderly it is especially important to evaluate hearing, vision, and cognitive ability. When cognitive impairment occurs in association with dementia, one is naturally lead to consider Alzheimer's disease, multi-infarct dementia, and subcortical dementing diseases.

Sometimes, however, apathy or other evidence of personality change may be the first indication of illness. Discovering the cause of apathy is more difficult in such situations. As a general principle, it is important to keep in mind that change in personality is very unusual in adulthood. While some individuals may make changes in their life style—for example, as part of the so-called midlife crisis or in response to the financial or environmental restrictions of retirement—persistent changes in motivational or emotional behavior are warning signs that a clinical problem is present (55). When there is suspicion of such clinically significant behavioral change, the patient should undergo full medical and neurological evaluation. In addition to a brain-imaging procedure and EEG, lumbar puncture and neuropsychological testing should be considered. Right hemisphere lesions may produce apathy or indifference with few elementary sensory or motor abnormalities. The diagnosis will be supported by a history of left-side sensorimotor symptoms or by neuropsychological evaluation that shows denial of illness (anosognosia), difficulty in getting dressed, visuospatial impairments, or neglect of the left side of space (56).

More difficult to recognize are syndromes of personality change associated with frontal lobe disease. Apathy in association with euphoria, irritability, impulsivity, and loss of social graces suggests frontal lobe disease. Specific neuropsychological testing for frontal lobe capacities, frontal release signs, and evidence of olfactory or visual field abnormalities may be helpful (40, 56). It is important not to rely unduly on brain-imaging procedures, since inflammatory conditions, such as syphilis, acquired immune deficiency syndrome, and granulomatous diseases, may affect the frontal lobe without producing detectable structural changes.

## TREATMENT AND RESEARCH IMPLICATIONS

The causes of apathy have been classified here as psychosocial, environmental, and biomedical. A rational approach to the treatment of apathy is based in part upon this classification. In addition, when apathy is secondary to a diagnosable disorder, treatment is built around diagnosis of that disorder. In such cases the heuristic value of apathy lies in its ability to facilitate accurate assessment. In practice the two approaches are complementary.

When apathy represents a response to stable but inadequate rewards or incentives, interventions can be directed at the social or physical environment. In some instances, such as social loss or deprivation, social or political initiatives are called for. These cases, therefore, are not conventionally seen as part of the clinician's responsibility to the patient. On the other hand, it is evident that when there are such concerns, ethical issues need to be considered in defining the extent of clinicians' responsibilities. In a more restricted sense, however, apathy as a response to social deprivation certainly calls on clinicians to initiate involvement of the available community resources. Cases of neglect of children or elderly persons represent fairly common instances in which such social management is an important part of care. They illustrate an important way in which the recognition of apathy as a sign of dysfunction may have heuristic value.

When apathy, despair, or demoralization occurs in the wake of personal or natural catastrophe, there are many individual and social interventions that may be considered (57). In general, they entail marshaling help from external resources and responding to the individual, family, or community sense of powerlessness, loss, and anger.

Treatment of apathy arising from cognitive, perceptual, or sensorimotor impairment entails two aspects: first, ensuring optimal treatment of the patient's hearing, visual, or elementary sensorimotor problems and, second, taking steps to match the patients' social and physical environment to any residual impairments. Supportive individual therapy can be useful. It is important to pay attention to family or other caregivers. Inactivity, which is often the cardinal sign of apathy, may be mistakenly judged as unchangeable when there are physical deficits that can explain it. As a consequence, reversible sensory or cognitive loss may be overlooked. Caregivers may also invoke psychological explanations that interfere with care and interpersonal relationships. For example, sometimes apathy will be viewed as willful, in which case the caregiver may become angry with the patient. A variation of this is projecting one's own anger onto the patient and then viewing the inactivity as the patient's way of showing anger, a problem particularly likely to occur when the patient has expressed anger indirectly in the past. More generally, when apathy results from an otherwise unrecognized medical problem (e.g., apathetic hyperthyroidism), evaluation will lead to specific medical treatment. When it results from some irreversible medical or neurological disease, the ability to label apathetic behavior as such will help patients or family members to understand and cope more effectively with the ambiguities or frustrations that arise from seeing previously competent individuals fail to initiate new goals or persevere at their previous activities.

Currently, the treatment for apathy secondary to major psychiatric disorders usually entails treatment directed at the primary diagnosis. However, in the case of schizophrenia, research targeting negative symptoms represents a specific attempt to treat apathetic states pharmacologically (24, 25). The use of methylphenidate to treat apathy in demented elderly patients (58) and the evaluation of motivational change in Parkinson's disease patients treated with dopamine agonists (52) may also be viewed as attempts to manipulate neural subsystems involved in producing apathy. In effect, these approaches suggest the possibility that apathy is a dimension of behavior having its own neurobiological substrates which may be modified for clinical purposes. If this is the case, treatments found effective for apathy in some conditions might be generalized to other disorders capable of producing apathetic states by similar mechanisms. Viewing apathy as a dimension of behavior having its own mechanisms also raises the possibility that when it occurs as a symptom in association with other syndromes, such as depression or akinesia, apathy may represent a behavioral feature having specific implications regarding mechanism or treatment.

The study of apathy may have additional value for clinical research and treatment. Apathy serves as a heuristic concept to help us examine the mechanisms by which actual or perceived changes in the physical or social environment lead to motivational impairment. Most of the disorders accompanied by apathy involve neural systems known to be important in the elaboration and control of emotion and motivation, such as the midbrain, diencephalic, frontal, and temporal subsystems that constitute the limbic system. In biochemical terms, many of the conditions that produce apathy affect catecholamines. In particular, hypofunction of dopaminergic systems has been postulated to play a central role in many of the conditions discussed (e.g., postpsychotic depression, depression, Parkinson's disease, frontal lobe syndrome, type II schizophrenia, pseudohypoparathyroidism, neuroleptic-induced akinesia, and amphetamine or cocaine withdrawal). These neurobehavioral and biochemical correlations are consistent with the concept that apathy is a state of primary motivational impairment. They suggest that the study of apathetic states may contribute to our understanding of the neurobiology of motivation. Conversely, information about the socioenvironmental, psychological, or neural controls on motivation may help us develop effective treatments for apathetic states.

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**APPENDIX 1. Psychological and Clinical States That May Produce Apathy Syndromes**

Schizophrenia (type II or negative symptoms)
Frontal lobe injury
Postpsychotic depression
Frontoparietal right hemisphere infarction
Cingulate gyrus/supplementary motor area infarction
Amphetamine or cocaine withdrawal
Other states of catecholamine hypoactivity, especially dopaminergic hypoactivity, e.g., neuroleptic-induced akinesia
Loss of environmental incentive or reward, as in role loss, institutionalization, and other states of environmental deficiency
Loss of elementary sensory or motor capacity, including hearing or vision
"Apathetic" hyperthyroidism

# Natural History of Male Psychological Health, XII: A 45-Year Study of Predictors of Successful Aging at Age 65

**George E. Vaillant, M.D., and Caroline O. Vaillant, M.S.S.W.**

*In order to determine important predictors of psychosocial and physical vitality in late midlife, the authors examined the lives of 173 men prospectively studied from ages 18 to 65. Biopsychosocial predictors—gathered before age 50—were examined for their correlation with three outcome variables measured at age 65: physical health, mental health, and life satisfaction. Extent of tranquilizer use before age 50 was the most powerful negative predictor of both mental and physical health outcomes at age 65. Another important predictor for* mental *health was maturity of defenses before age 50. Paradoxically, warm childhood environment made an important independent contribution to predicting* physical*—not mental—health.*

(Am J Psychiatry 1990; 147:31–37)

Fifteen years ago the senior author operationally defined a concept of mental health based on the lives of male college sophomores studied from ages 18 to 47 (1). In the intervening years these erstwhile college sophomores have now reached the age of retirement—65 years. The present study again examines their mental health but this time from the perspective of late midlife. To avoid the confounding effects of sex, socioeconomic class, and historical cohort, this research has focused on a very homogeneous sample of men and attempts only intragroup comparisons.

To avoid platonic definitions of mental health (e.g., Jahoda [2] and Maslow [3]), this report will use "operational referents," as suggested by Grinker et al. (4) in their pioneering work on "homoclites." Thus, to identify the most promising predictors of late-life adaptation, this study asked three separate, if intercorrelated, questions about the study members who survived until age 65: 1) Who remained in excellent physical health? 2) Who required no recourse to mental health professionals and showed clear ability to play and to work and to love? 3) Who regarded the last decade as the happiest of their lives? This report seeks the predictors of such successful late midlife outcomes.

## METHOD

### *Sample*

Between 1940 and 1942, the Harvard University Health Services chose 204 white college sophomores for intensive multidisciplinary study. The men had been originally selected because their freshman health service physical examination had revealed no mental or physical health problems, and their college deans saw the men as becoming promising adults (5, 6). The men were reinterviewed at age 25 years, at age 30, and again between ages 47 and 57. For 45 years or until their death, the men have been studied prospectively by means of annual or biennial questionnaires. Physical examinations have been obtained every 5 years. By design, most ratings have been derived from raters who were blind to other assessments.

Of the 204 men originally in the sample, six had dropped out in college; 23 men had died before age 60, and two had data sets too incomplete to rate for mental health. This attrition left 173 active study members whose late midlife psychosocial adjustment could be adequately assessed. We evaluated the sample accord-

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**TABLE 1. Intercorrelation of the Nine Items of the Psychosocial Adjustment Scale (ages 50–65 years) and Their Association With the Outcome Variables for 173 Men**

| Measure | Spearman Correlation Coefficient ($r_s$)[a] 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 |
|---|---|---|---|---|---|---|---|---|---|
| Scale item | | | | | | | | | |
| 1. Continued employment (1=full, 3=retired) | | | | | | | | | |
| 2. Sustained job success (1=yes, 2=no) | 0.34[b] | | | | | | | | |
| 3. Job/retirement satisfaction[c] | 0.31[b] | 0.37[b] | | | | | | | |
| 4. 3+ weeks of vacation (1=yes, 2=no) | −0.16 | 0.11 | 0.16 | | | | | | |
| 5. Few psychiatric visits (1=0, 3=>10) | 0.05 | −0.03 | 0.02 | −0.13 | | | | | |
| 6. Little tranquilizer use[d] | 0.15 | 0.18[b] | 0.16 | −0.02 | 0.42[b] | | | | |
| 7. <5 sick days/year (1=yes, 2=no) | 0.07 | 0.21[b] | 0.19[b] | 0.02 | 0.10 | 0.34[b] | | | |
| 8. Marital satisfaction[c] | 0.04 | 0.07 | 0.16 | 0.00 | 0.32[b] | 0.24[b] | 0.10 | | |
| 9. Recreation with others (1=yes, 2=no) | 0.03 | 0.23[b] | 0.11 | 0.18[b] | 0.13 | 0.10 | 0.00 | 0.02 | |
| Global outcome variable | | | | | | | | | |
| Psychosocial adjustment at ages 50–65 | 0.48[b] | 0.46[b] | 0.51[b] | 0.19[b] | 0.48[b] | 0.61[b] | 0.36[b] | 0.56[b] | 0.34[b] |
| Objective physical health | 0.09 | 0.25[b] | 0.20[b] | 0.01 | 0.21[b] | 0.31[b] | 0.23[b] | 0.17 | 0.20[b] |
| Observer-rated life satisfaction | 0.20 | 0.45[b] | 0.49[b] | 0.13 | 0.14 | 0.38[b] | 0.32[b] | 0.34[b] | 0.20[b] |
| Subject-rated life satisfaction (happiness) | 0.14 | 0.25[b] | 0.30[b] | 0.00 | 0.01 | 0.18[b] | 0.22[b] | 0.23[b] | 0.03 |

[a] If $r_s > 0.13$, $p < 0.05$.
[b] $p < 0.01$. If $r_s > 0.23$, $p < 0.001$.
[c] 1=clear satisfaction, 2=ambiguous, 3=clear dissatisfaction.
[d] Maximum yearly use of hypnotics, tranquilizers, and antidepressants; 1=<5 days, 2=5–30 days, 3=>30 days.

ing to three measures: outcome variables, early predictor variables, and later predictor variables.

### *Outcome Variables*

*Objective physical health.* Each man's physical examination, obtained at mean±SD age 63±1 year, was rated by an internist who was blind to other assessments (physical health still excellent=1; minor irreversible problems [e.g., glaucoma, gout]=2; irreversible life-shortening chronic illness=3; chronic illness and disability=4; dead=5). The scale is described in greater detail elsewhere (7).

*Psychosocial Adjustment Scale, ages 50 to 65 years.* The scale closely follows scales designed to assess mental health at age 47 (1, 7). On the basis of seven questionnaires, two wives' questionnaires, and, for 58%, personal interviews during the last 15 years, the men were rated on nine variables. The variables and their weighting are described in table 1. The points from the nine items were summed to provide a continuous measure of late midlife psychosocial adjustment. A low score reflected positive mental health. On individual items interrater reliabilities ranged from 0.47 to 0.85. Rater reliability for the total adjustment scale was 0.86.

*Life satisfaction: observer rated.* On the basis of the blind raters' review of all questionnaires and interview data for the age period 50–65 and discounting distress from purely physical disability, the raters assessed how satisfied the men appeared with this period of their lives. Would the rater have been satisfied to "walk in their moccasins" (1=clearly satisfied, 3=ambiguous, 5=clearly unhappy)? Rater reliability was 0.65.

*Life satisfaction: subject rated.* In 1977 and 1983 (at about ages 56 and 62, respectively) the men were asked to state which of the five preceding 7-year periods of their adult lives was the happiest and which of the five periods was the unhappiest (1=subject ranked the most recent 7-year period as the happiest [N=63], 2=present period not specified or both questionnaires not returned [N=79], 3=present period ranked as the unhappiest [N=31]).

### *Early Predictor Variables*

*Childhood strengths (ages 0–18 years).* Two research assistants who were blind to data gathered on the subjects after age 20 reviewed 10–20 hours of social history gathered from the subjects and their families. They rated the men on eight subscales, which are described in detail elsewhere (8). A low score on the sum of the eight scales indicated familial cohesion, good relations with parents, and an absence of childhood emotional problems. Interrater reliability was 0.71.

Three of the eight subscales were also used as independent variables. For each subscale the two independent raters' scores of 0–2 were summed, giving a range of 0–4.

1. *Childhood emotional problems (ages 0–14 years)* (2=presence of phobias, fearfulness, social with-

drawal, or behavior problems; 1=rater uncertainty; 0=a clearly well-adjusted childhood).

2. *Closeness to siblings* (2=distant or destructive relationship or no siblings; 1=rater uncertainty; 0=close, enjoyable relationship with at least one sibling).

3. *High school adjustment* (2=marked social problems; 1="average" social adjustment, no team activities; 0=social success with participation in competitive sports or academic success).

*Standing pulse rate in college.* The men in college received a complete physical examination and physiological study in an exercise laboratory. Resting pulse rate was taken in standing, sitting, and recumbent positions.

*Psychosocial adjustment, ages 18–22 years.* After 3 years of study, by staff consensus each subject was rated on an ABC scale of "psychological soundness" (score of 1 to 3; C, or 3, indicated a categorical judgment of "definite handicap."

*College traits.* At the end of college, a psychiatrist reviewed all of the data gathered on the men during the previous 3 years (9). He then assigned to each man several of 26 selected personality traits (rating: 1=absent, 2=present). Rater reliability was not sought. Of the 26 traits, only two significantly predicted future mental health. These were:

1. *Practical-organizing.* "Not theoretical, speculative, or scholarly. Their interests are more practical, and in their course work they are better in organization than in analytic or creative work . . . essentially pragmatic" (5, pp. 26–27).

2. *Well-integrated.* "Steady, stable, dependable, thorough, sincere and trustworthy . . . factor that enables a young man to surmount common problems" (5, p. 23).

Three other traits had been highly correlated with psychosocial adjustment in college. These were:

3. *Vital affect.* "Vitality and richness of affect . . . spontaneous force and energy . . . richer verbal expression, greater animation" (5, p. 24).

4. *Friendly-sociable.* "Naturally friendly, makes friends easily . . . unhampered by shyness or awkwardness" (5, p. 28).

5. *Psychiatric impairment.* "Psychopathic" trait was assigned to 13 of the 204 men whom the staff research psychiatrist deemed categorically psychiatrically impaired.

*Parental socioeconomic class.* This was estimated by the 5-point classification devised by Hollingshead and Redlich (10).

*Exercise in college.* In college, average number of hours of weekly exercise had been assessed (1=more than 10 hours of exercise a week, 2=2–9 hours a week, and 3=less than 2 hours a week).

*Psychosocial adjustment, ages 22–29 years.* After 10 years of study and review of all available data, the original study director, Clark Heath, classified each subject on a 5-point scale of "personality stability." A rating of 1 indicated an unusually stable personality and 5 a clearly unstable personality.

### *Later Predictor Variables (ages 30–50)*

*Psychosocial adjustment (ages 30–47 years).* In 1972, a rater who was blind to other ratings assessed the men, at the mean age of 47±2 years, on a scale that included seven relatively objective, longitudinally derived measures of psychosocial adjustment. These measures were steady occupational advancement, recreation with others, more than 2 weeks of enjoyable vacation annually, less than 5 days of sick leave annually, earned income of more than $20,000 a year (1968 dollars), marital satisfaction, and occupational satisfaction. (The strong association of these seven measures with alternative definitions of mental and physical health has been documented during the subsequent 15 years of data analysis [1, 7, 11].) A low score reflected positive mental health.

*Mood-altering drug use before age 50 (maximum yearly use)* (1=less than 5 days' use of sleeping pills, tranquilizers, or antidepressants; 2=maximum of 5–30 days of use; 3=more than 30 days of use; 4=social or health damage due to mood-altering drug use).

*Alcohol abuse.* This was rated (1=absent, 2=present) by a rater who was blind to other data. "Abuse" was defined as either the subject's concern over his control or concern by others about the subject's control over alcohol use or "many drinks" a day at two points in time. Fifteen years of follow-up and interview have documented the validity of this estimate by a blind rater.

*Maturity of defenses.* This was assessed by a 9-point scale (1=mature, 9=immature). Examples of adaptive behavior at times of crisis and conflict were excerpted as vignettes. On the basis of a glossary, each vignette was labeled as one of 15 different defenses. These 15 defense headings were grouped as follows: immature (schizoid fantasy, projection, passive aggression, hypochondriasis, acting out, and dissociation), intermediate (intellectualization/isolation, repression, displacement, and reaction formation), and mature (sublimation, suppression, anticipation, altruism, and humor). Interrater reliability for scaling maturity of defenses in this manner ranged from 0.72 to 0.84. Methods, rationale, and reliability are described in detail elsewhere (6, 12, 13).

*Depression.* Unlike other assessments, depression was rated in a nonblind manner. The senior author, having reviewed the men's records for 20 years, judged if the subject met the criteria for major depression or dysthymia before age 50 (1=yes, 2=no).

*Overweight at age 50.* Each man's Quetelet index ($kg/M_2$) was calculated. If the index exceeded 25.0, the man was classified as overweight (14).

*Smoking.* The men's smoking histories were obtained from biennial questionnaires from ages 2[illegible] to 50 and were rated as follows: 1=never smoked, 2=1–10 pack/years or pipe smoker, 3=11–29 pack/years, 4=30–49 pack/years, 5=50 or more pack/years (15).

*Mean ancestral longevity.* The age at death of each man's four grandparents and two parents were summed and divided by six (range=57–88).

## RESULTS

Table 1 illustrates the intercorrelation of the variables making up the Psychosocial Adjustment Scale. The first two items reflect the men's ability to work, the next two items their ability to play, the next three items—mood-altering drug use, use of a psychiatrist, and days of sick leave—their emotional well-being, and the last two items the men's ability to love. Analogous to individual performance on the events in a decathlon, these items were only weakly correlated with each other. However, almost all items correlated significantly with more global assessments of mental health. Expressed differently, all but two of the nine criteria (vacations and recreation) were "failed" *10* times as often by the 44 men with the worst outcomes as by the 51 with the best outcomes. Subject-rated happiness was less highly correlated with the individual items on the Psychosocial Adjustment Scale than was physical health or observer-rater happiness. Unlike more objective measures of physical and psychosocial adjustment at age 65, subject-rated life satisfaction was *not* predicted by such obvious premorbid variables as childhood environment, depression, use of a psychiatrist, alcohol abuse, or past marital enjoyment.

Between age 50 and age 65 there was a progressive decline in the physical health of the 188 men who had survived until age 45. At age 40, 151 men had been in excellent health. At age 50 the number in excellent health had declined to 91, but only 22 men were rated as chronically ill. By age 63±1, only 41 men remained in excellent health, i.e., still revealed no evidence of significant, irreversible illness or physical defect. Sixty-nine men had become chronically ill or died.

On the one hand, poor psychosocial adjustment appeared to play an etiologic role in the observed decline in physical health. For example, 15 of the 21 men given a diagnosis of dysthymia or major depression before age 50 were chronically ill or dead by age 63. On the other hand, poor physical health undoubtedly also played an etiological role in decline in late midlife psychosocial adjustment. Therefore, in table 2, before the correlation of premorbid variables with psychosocial adjustment was calculated, the association of such variables with future decline in physical health was controlled. However, even when this precaution was taken, the same early life variables that predicted sustained excellent physical health also predicted psychosocial vitality. Surprisingly, the most significant predictor of both physical and mental ill health at age 65 was mood-altering drug use before age 50.

Presence of childhood strengths was clearly associated with health at age 65. Before age 50, the most powerful predictive subscales of this scale were the cohesiveness of the home and whether or not the boy's relationships with his mother and father were conducive to trust, autonomy, and initiative (8). However, at age 65 the single item of closeness to sibs (rated 0–2)—a subscale that at earlier ages had not been significantly correlated with psychosocial outcome—became as powerful a predictor of late life adjustment as the full 20-point childhood adjustment scale. By way of illustration, 12 (52%) of the 23 men with a lifetime diagnosis of depression, but only three (7%) of the 44 men with the best psychosocial outcome, were noted in college to be only children or estranged from siblings.

**TABLE 2. Predictors of Successful Late Midlife Adjustment of 173 Men**

| Predictor | Correlation Coefficient: Physical Health at Age 63[a] | Correlation Coefficient: Psychosocial Adjustment at Age 65[b] | Correlation Coefficient: Observer-Rated Satisfaction at Age 65[a] |
|---|---|---|---|
| Before age 20 | | | |
| Childhood strengths | 0.26[c] | 0.12 | 0.24[c] |
| Closeness to sibs | 0.18[d] | 0.17[d] | 0.22[e] |
| "Well-integrated" in college | 0.10 | 0.23[c] | 0.20[e] |
| Before age 50 | | | |
| Mood-altering drug use | –0.36[c] | –0.46[c] | –0.30[c] |
| Number of psychiatric visits | –0.14[d] | –0.40[c] | –0.17[d] |
| Alcohol abuse | –0.23[c] | –0.22[e] | –0.22[e] |
| Pack/years of smoking | –0.13[d] | –0.26[c] | –0.16[d] |
| Overweight at 50 (Quetelet Index) | –0.14[d] | –0.13[d] | –0.22[e] |
| Days of sick leave/year | –0.16[d] | –0.21[e] | –0.19[e] |
| Maturity of defenses at ages 20–47 | 0.19[e] | 0.41[c] | 0.36[c] |
| Suppression (major defense) | 0.03 | 0.27[c] | 0.22[e] |
| Good psychosocial adjustment at age 47 | 0.19[c] | 0.45[c] | 0.31[c] |

[a] Statistical significance based on Spearman correlation coefficient ($r_s$).

[b] In the assessment of the correlations between predictor variables and late midlife psychosocial adjustment, the effects of physical health at age 63 were partialled out. This procedure necessitated using Pearson correlation coefficients (r).

[c] $p<0.001$.

[d] $p<0.05$.

[e] $p<0.01$.

Of the 41 men who remained in excellent physical health, 63% (N=26) manifested two or more of the following variables: warmth of childhood—top quartile, longevity of ancestors—top quartile, college diastolic blood pressure lower than 66 mm Hg, and more than 10 hours/week of college exercise. Only 14% (N=4) of the 29 men who died before age 65 manifested two or more of these variables. Twenty-three of the original 204 men had been excluded from this follow-up because they died before age 60. The 10 deaths before age 45 were "acts of God," e.g., polycystic kidney, World War II combat, blameless accident. Of the 13 deaths after age 45 but before age 60, two could be attributed to alcohol abuse and three to suicide; and three more of these men met criteria for a *DSM-III* diagnosis.

Table 3 illustrates that many variables often thought

**TABLE 3. Theoretically Important Variables That Did Not Predict Outcome in Late Midlife for 173 Men**

| | Spearman Correlation Coefficient ($r_s$) | | |
|---|---|---|---|
| Variable | Physical Health at Age 63 | Psychosocial Adjustment at Age 65 | Observer-Rated "Happiness" at Age 65 |
| Not important for outcome | | | |
| Childhood socioeconomic class | 0.03 | 0.04 | 0.01 |
| Stability of parental marriage | 0.05 | 0.11 | 0.08 |
| College scholastic aptitude | −0.02 | 0.07 | 0.02 |
| Childhood emotional problems | −0.05 | −0.09 | −0.17[a] |
| Psychiatric impairment in college | −0.02 | −0.05 | −0.08 |
| "Vital affect" in college | 0.01 | 0.04 | 0.10 |
| "Friendly, sociable" in college | 0.01 | 0.04 | 0.06 |
| Not important for physical health | | | |
| Low standing pulse rate | 0.08 | 0.24[b] | 0.26[b] |
| Regular exercise in college | 0.09 | 0.18[a] | 0.15[a] |
| College psychosocial adjustment score | 0.05 | 0.16[a] | 0.10 |
| Psychosocial adjustment score at age 29 | 0.01 | 0.22[c] | 0.16[a] |
| "Practical-organizing" in college | 0.04 | 0.21[c] | 0.05 |
| Not important for psychosocial adjustment | | | |
| Mean ancestral longevity | 0.16[a] | 0.07 | 0.07 |
| Number of octogenarians | 0.18[c] | 0.12 | 0.03 |
| Number of nonagenarians | 0.19[c] | 0.11 | 0.14[a] |
| Years of orphanhood before age 18 | −0.15[a] | 0.03 | 0.06 |

[a] $p<0.05$.
[b] $p<0.001$.
[c] $p<0.01$.

to be associated with adjustment in young adulthood (e.g., childhood socioeconomic class, loss of parent by death ("orphanhood"), college scholastic aptitude) were uncorrelated with late life outcome. Similarly, extroverted personality variables such as sociability and vital affect, which were strongly associated with good psychological adjustment in college and young adulthood, did not predict mental health for this sample in late midlife.

A few predictor variables had a statistically significant association with one outcome but not the other. The variable most clearly associated with good psychosocial adjustment at age 65, but not physical health at age 63, was good psychosocial adjustment in young adulthood. A low standing pulse in college was another relatively strong early predictor of successful late midlife psychosocial, but not physical, health. (Previous work [16] had demonstrated that this association was independent of physical fitness.) Hereditary longevity was a significant predictor of physical, but not psychosocial, vitality in late midlife.

**TABLE 4. Independent Contribution of Predictor Variables in Explaining Physical Health and Psychosocial Adjustment of 164 Men[a] at Late Midlife**

| | Partial Correlation of Each of Six Predictor Variables With the Other Five Controlled (r) | |
|---|---|---|
| Variable | With Physical Health at Age 63 | With Psychosocial Adjustment at Ages 50–65 |
| Mood-altering drug use before age 50[b] | −0.29[c] | −0.49[c] |
| Maturity of defenses at ages 20–47[b] | 0.04 | 0.37[c] |
| Childhood strengths | 0.20[c] | 0.01 |
| Alcohol abuse before age 50 | −0.16[d] | −0.14[d] |
| Vigorous exercise in college | 0.10 | 0.21[e] |
| Ancestral longevity | 0.13[f] | 0.04 |

[a] N=164 due to missing data for some subjects.
[b] Depression or number of psychiatric visits could have been substituted for use of tranquilizing drugs and psychosocial adjustment at age 47 substituted for maturity of defenses with almost the same results.
[c] $p<0.001$.
[d] $p<0.05$.
[e] $p<0.01$.
[f] $p=0.06$.

Table 4 depicts examination of the unique importance of each of six of the most robust predictors of health in tables 2 and 3 when the other five were controlled. Table 4 confirms the negative implications of mood-altering drug use. Surprisingly, childhood strengths explained additional unique variance in predicting physical health but not psychosocial adjustment. After other variables were controlled, maturity of ego defenses, assessed before age 50, made the greatest independent contribution to psychosocial adjustment in late midlife.

At several points in adult development, independent raters made global assessments of the men's psychosocial adjustment. Table 5 illustrates that with the passage of time, not surprisingly, clear shifts occurred. Thus, there were only 15 of the 173 men who at every period of observation were placed in the top quartile of adaptation. Perhaps the two most important variables in causing shifts from good adjustment at ages 18–30 to poor psychosocial adjustment at ages 50–65 were the onset of poor physical health and alcoholism.

The reasons for improvement in psychosocial adjustment from poor adjustment in youth to good adjustment in late life were less apparent. However, three college "protective" variables that became more salient with the passage of time were closeness to siblings, low college standing pulse, and the trait of practical-organizing. Another reason was that as men grew older the detrimental effects of personality disorder became less apparent. For example, the college trait of psychopathic correlated with college psychosocial adjustment (r=0.33, N=173, $p<0.001$) and adjustment in young adulthood (r=0.26, N=173, $p<0.001$); but

**TABLE 5. Intercorrelation of Psychosocial Health Scale Scores Over the Life Span for 173 Men**

| | Spearman Correlation Coefficient ($r_s$) | | | | | |
|---|---|---|---|---|---|---|
| Psychosocial Adjustment Scale (range)[a] | 1 | 2 | 3 | 4 | 5 | 6 |
| 1. Ages 2–14, emotional problems (0–4) | | | | | | |
| 2. Ages 14–18, high school adjustment (0–4) | 0.22[b] | | | | | |
| 3. Ages 18–22 (1–3) | 0.30[c] | 0.34[c] | | | | |
| 4. Ages 22–29 (1–5) | 0.28[c] | 0.21[b] | 0.59[c] | | | |
| 5. Ages 30–47 (7–16) | 0.20[b] | 0.21[b] | 0.24[b] | 0.35[c] | | |
| 6. Ages 50–65 (9–21) | 0.09 | 0.09 | 0.16[d] | 0.22[b] | 0.48[c] | |
| 7. Ages 57–62, subject-rated life satisfaction (1–5) | 0.13[d] | 0.07 | 0.09 | 0.10 | 0.14[d] | 0.33[c] |

[a] Low end of each scale equated with health.

[b] $p<0.01$.

[c] $p<0.001$.

[d] $p<0.05$.

the trait was not correlated with any important outcome variable at age 65.

## DISCUSSION

This sample of 173 men was a favored one. They were white men selected for good physical health and high academic achievement. Most men received some graduate education, and all had forged their occupational careers during a time of American economic growth and prosperity. They had access to good medical care and nutritional practices and the opportunity for exercise. At 65 their mortality was only half that of white American men of the same birth cohort. But in multivariate analysis, homogeneity of sample has advantages.

In the present study, five overarching variables seem of probable major etiologic importance to late life adjustment. These five variables were long-lived ancestors (for physical health only), sustained familial relationships (prior closeness to parents was important in young adulthood, prior closeness to siblings looming more important in late midlife), maturity of defenses, absence of alcoholism, and absence of depressive disorder.

In table 4 mood-altering drug use was substituted for clinical diagnosis of depression because the independent rating of drug use could be separated from halo effects. In this study and perhaps in other non-drug-abusing samples, tranquilizer use may serve as an objective marker for both depression and alcoholism, with which it was highly correlated. Multivariate analysis confirmed that the association of depression with poor health could not be fully explained by suicide, smoking, and alcohol abuse.

The relevance of a cohesive childhood to successful aging is probably multifaceted. First, as Rowe and Kahn (17) suggest, the capacity for good self-care and self-esteem often makes the difference between being "old" and being "sick." Men with good psychosocial adjustments at age 65 were much more likely to have never smoked or, if they began, to have stopped. In college they were twice as likely to have completed the treadmill run and be deemed "steady and dependable" and "practical-organizing." Suppression—the capacity to postpone but not forgo gratification—was more common. The traits of minimal smoking, college treadmill run, and being deemed practical and stoical were all significantly associated ($p<0.01$) with childhood strengths.

Second, although bleak childhood did not predict alcohol abuse (6, 8, 18), it did predict depression. Since quality of childhood was largely based on data from the men's parents, gathered when the men were age 18 years, the association of bleak childhood with adult depression was not due just to pessimistic attribution style. Only five of the 21 men clinically judged by the senior author as meeting the criteria for depressive disorder *before age 50* had not been ranked by blind raters in the *bottom* quartile in childhood strengths, childhood emotional stability, or soundness in college.

A major difficulty in life span developmental studies has been to distinguish causal linkages between precursors and outcome variables from mere statistical associations. Our small sample size and large number of variables have limited the usefulness of sophisticated multivariate modeling procedures. For example, our data do not allow the variance contributed by external manifestations of mental illness (e.g., psychiatric diagnosis or mood-altering drug use) to be dissected from the variance contributed by intrapsychic ego strength (e.g., maturity of defense mechanisms). Most likely, they are opposite sides of the same coin. Nor do our data allow clarification of the observed importance of siblings and low standing pulse to late life outcome. Are these merely spurious associations significant by chance in a multivariate study, or are they adolescent indicators of stable family relationships and low social anxiety (Kagan et al. [19]), respectively, that truly affect late midlife adjustment? Clearly, replication is needed.

However, questions of etiology in life span development cannot even be asked until long-term univariate associations are identified. In addition, table 3 suggests that many potential causal factors were not important. In keeping with some evidence (20, 21), parental death, per se, did not predict subsequent depression or poor late midlife psychosocial adjustment. Nor was outcome at age 65 correlated with extroverted college personality variables—variables that had been strongly associated with mental health in young adulthood (5, 9). For example, the trait sociable, "general ease in social relationships," correlated with good adjustment in college ($r=0.24$, $N=173$, $p<0.001$), and vital affect correlated with good adjustment in college ($r=0.31$, $N=173$, $p<0.001$) and in young adulthood ($r=0.18$, $N=173$, $p<0.02$). Yet these traits were not associated with late life outcome. The most likely explanation is that during the adult life span the social skills of the eccentric and of the isolated men continued to improve, while simultaneously alcohol abuse afflicted the extroverted, if anything, more than the introverted. Thus, table 5 offers hope that personality disorder, like adolescence, may sometimes be a self-limiting disorder. The race, as Ecclesiastes and Aesop remind us, is not always to the swift.

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# Medicine Court, II: *Rivers* in Practice

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*The authors conducted a retrospective study of the initial impact (1986–1987) of the* Rivers v. Katz *decision involving patients' right to refuse treatment at New York State's largest forensic psychiatric hospital. Of 18 petitions submitted, 15 cases were adjudicated. All 15 patients were found incompetent, and all treatment plans submitted were approved by the court. Most patients selected for* Rivers *hearings were diagnosed as having chronic schizophrenia and/or were older than the hospital population. A comparison of the implementation of the* Rivers *decision with that of* Rogers v. Commissioner of Mental Health *in Massachusetts showed* Rogers *to be significantly more expensive in human resources, time, and money.*

(Am J Psychiatry 1990; 147:38–43)

In 1986, New York joined the ranks of those states which prohibit unilateral administrative procedures for the determination of a patient's competency to make decisions regarding psychiatric treatment. This case law is known as the *Rivers v. Katz* decision (1). The Court of Appeals of the State of New York (the state's highest court) held that administrative review of a patient's competency to make informed judgments concerning psychiatric treatment did not adequately protect the patient's right to due process, as delineated in the New York State Constitution (article I, 96).

Previously in New York, the administrative review for the purpose of initiating treatment over a patient's objection involved an analysis of the objection by the chief of the service and the opportunity for the patient to appeal to both the facility director and the regional director. The law also provided for the patient's right to legal counsel throughout these procedures (14 NYCRR 27.8). In the *Rivers* case, Mark Rivers had been involuntarily committed to the Harlem Valley Psychiatric Center by order of the Duchess County Court, pursuant to Mental Hygiene Law 9.01. His objection to proposed treatment with antipsychotic medications led to the implementation of the administrative procedures that ultimately overruled his objections. He was then forcibly administered antipsychotic medications, including fluphenazine hydrochloride, fluphenazine decanoate, and thioridazine.

During the administrative review and subsequent unsuccessful appeal to the lower courts by Rivers, the representatives of the treating psychiatrists relied on the state's *parens patriae* interests in overruling Rivers' objections to treatment, citing his commitment to the psychiatric hospital as evidence of his incompetency to determine the treatment he should receive. The court, although conceding that compelling state interests may properly lay the groundwork for *parens patriae* actions, specifically rejected the psychiatrists' argument equating involuntary commitment with patient incompetency to make treatment decisions. In addition, the court criticized the administrative process and listed several specific objections, including the lack of standards and criteria to establish the need for medication, the failure to designate the duration of a forced-medication order, and the absence of a requirement that the medication be evaluated as to its intrusiveness and the possibility of adverse side effects.

On the basis of these objections to the administrative review process, the court held that a declaration of incompetency to make a treatment decision "is uniquely a judicial, not a medical function," thus necessitating the involvement of the courts in forced-medication cases relying on *parens patriae* interests (1). (Forced medication in emergency situations, such as when there is imminent danger to the patient or to those in the immediate vicinity, invokes the state's police powers and remains justifiable when the state's interests are compelling [1].) Furthermore, the proposed treatment must meet certain criteria: 1) the patient's liberty interests must be recognized, 2) the patient's best interests must be considered, 3) the benefits that the patient could enjoy must be clearly defined, and 4) an evaluation of any less intrusive alternative treatments must be presented. Thus, the courts have ruled not only that the patient must be ruled incompetent judicially but also that the proposed treatment must be approved judicially.

The 1982 *Rogers v. Commissioner of Mental Health* decision in Massachusetts dealt with similar common law issues (2). The courts of both New York and Massachusetts have rejected state claims equating involuntary commitment to a psychiatric facility with incompetency to make a treatment decision. Both states also

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**TABLE 1. Rulings of New York in the *Rivers* Decision and of Massachusetts in the *Rogers* Decision**

| | Ruling | |
|---|---|---|
| Aspect of Decision | *Rivers* | *Rogers* |
| Patients affected | Involuntarily committed patients who refuse medications and who may be incompetent | Involuntarily committed patients who may be incompetent, regardless of whether they accept recommended treatment |
| Factors considered in evaluation of treatment | Patient's liberty interests<br>Patient's best interests<br>Benefits expected with proposed treatment<br>Side effects<br>Evaluation of any less intrusive treatments | Patient's expressed wishes regarding medication<br>Effect on family<br>Prognosis without treatment<br>Prognosis with treatment<br>Side effects |
| Implementation | No guardian is appointed<br>Treatment plan is implemented with judge's order | Guardian is appointed to monitor court-ordered treatment plan<br>Guardian has right to challenge any change in treatment |

asserted the patient's right to a court hearing on the matter of competency. The rulings of the two states differ, however, with regard to the patients affected, the type of treatment, the evaluation of the treatment, and the implementation of the ruling (see table 1). The actual application of the *Rogers* decision at Bridgewater State Hospital, the largest forensic psychiatric hospital in Massachusetts, was reported by Veliz and James in 1987 (3). The purpose of this study is to report our experience with the *Rivers* opinion in practice at Central New York Psychiatric Center, the state's largest forensic psychiatric hospital serving sentenced patients, and to draw parallels and describe differences in the application of the *Rogers* and *Rivers* decisions.

## SETTING

The Central New York Psychiatric Center for the psychiatric treatment of the incarcerated is located in Marcy, N.Y. Three classes of prisoners are admitted to this facility: 1) convicted felons who reside in the state's correctional facilities (78%), 2) convicted county jail prisoners (8%), and 3) pre-trial or pre-sentence detainees from the county jail (14%). The average census is usually between 200 and 250 patients, all involuntarily committed. In the course of a year the facility admits approximately 1,200 patients, most of whom are acutely psychotic.

On admission to the center each patient receives a complete physical examination by a Board-certified family practitioner and a psychiatric evaluation by one of the staff psychiatrists. In cases of possible language difficulties, interpreters are present, and one of the psychiatrists is fluent in Spanish. The patient is further evaluated by a psychologist, a registered nurse, a social worker, an occupational therapist, and a recreational therapist. These evaluations are considered in the formulation of a treatment plan. Although less invasive treatments are extensively used, antipsychotic medications are prescribed in most cases of acute psychosis.

Central New York Psychiatric Center is affiliated with the State University of New York-Syracuse Health Sciences Center through the forensic fellowship program of the Department of Psychiatry. Based largely at the center, the participants in the fellowship program include a clinical director, an associate clinical director, and two fellows in training. The forensic psychiatric responsibilities, including those of the *Rivers* cases, are a function of the forensic program.

## PRE-COURT PREPARATION

If a psychotic patient refuses neuroleptic medication, the reason for this refusal is explored in depth by the psychiatrist and the entire support staff. The risks and benefits of the proposed medication are explained fully, and the patient's refusal may be discussed in the patient's group therapy sessions. When available, trusted family members may be asked to encourage the patient's compliance. If these avenues fail to convince the patient to comply with the proposed medication, a process that sometimes takes weeks, the treating psychiatrist may decide to pursue a forced-medication order. The process begins with written notification to the patient of the physician's intention to bring judicial action on the question of competency and the propriety of using antipsychotic medications. Copies of this notice are sent to the clinical director of the hospital and to the patient's legal representative. To ensure that all the information pertinent to the issues of competency and use of antipsychotic medication are evaluated and presented to the court, the New York State Office of Mental Health has developed a standardized evaluation form that includes 1) a clinical summary, 2) evaluations of the patient's competency, 3) a description and rationale of the proposed treatment, 4) a summary of the benefits and side effects the patient may encounter, and 5) evaluations of less invasive treatments.

The clinical director then requests a second psychiatrist to make a similar evaluation. If the second psychiatrist has a differing opinion as to the competency of the patient or on the treatment evaluation, a third staff psychiatrist's opinion is requested. The necessity for a third opinion did not occur during the first year of *Rivers* in practice. If the criteria for incompetency are met—i.e., the patient is irrational because of severe mental disorder, has little or no insight, and lacks the ability to make an informed decision with respect to therapy—a formal petition is then presented to the district's attorney general, who requests the court to schedule a hearing.

## METHOD

For each patient involved in a *Rivers* procedure, we established a separate file that included age, ethnicity, education, sex, psychiatric diagnosis (*DSM-III-R*), time required for court hearing, and professional medical time involved. In addition, we designed a flow sheet to facilitate the tracking of the various demographic data and court procedures. These data were then compared with the demographic profiles of all the patients admitted to Central New York Psychiatric Center for the year 1987 and with the data accumulated by Veliz and James in their study of the *Rogers* decision in Massachusetts (3). One of us (F.H.D.) attended five of the 15 *Rivers* hearings and interviewed six of the psychiatrists involved in these cases.

## RESULTS

During the first year of *Rivers* in practice at the psychiatric center, 18 petitions were submitted to the court. The language, race, sex, and diagnoses of these patients compared with the total population in the center (N=1,169) are presented in table 2. The 18 *Rivers* patients had a mean number of 10.6 years (range=8–15) of schooling, compared with 10.4 years (range=0–17) for the total population. Two important differences were seen between these two groups. First, the mean age of the *Rivers* patients—39.7 years (range=23–64)—was greater than that of the total population—31.8 years (range=17–74) ($Z=3.819$, $p<0.05$). Second, the *Rivers* patients had a greater rate of schizophrenic diagnoses and a lower rate of antisocial personality disorder (see table 2). Ten of the *Rivers* patients had concurrent axis II diagnoses, but in only two instances was this diagnosis cited as being a substantial threat to the patient's health or a condition that could be substantially exacerbated by the patient's disturbed mental state.

Of the 18 *Rivers* patients, 13 refused medication on the basis of denial of illness and four refused for reasons related to illogical or delusional thoughts. The remaining patient did not deny that he had psychiatric problems but denied the need for medication. Three of the *Rivers* petitions were withdrawn after these patients decided to comply with the recommended medication, and the remaining 15 proceeded to court hearings. Between the filing of the petition and the actual hearing, the average waiting time was 24 days (range=8–53). All of these patients had been involuntarily committed to the psychiatric center at the time of their *Rivers* hearings.

**TABLE 2. Characteristics of Patients in *Rivers* Petitions and All Patients in the Central New York Psychiatric Center in 1987**

| | *Rivers* Patients (N=18) | | All Patients (N=1,169) | |
|---|---|---|---|---|
| Item | N | % | N | % |
| Language | | | | |
| English | 18 | 100.0 | 1,052 | 90.0 |
| Spanish | 0 | 0.0 | 106 | 9.1 |
| Other | 0 | 0.0 | 11 | 1.0 |
| Race | | | | |
| White | 5 | 27.8 | 415 | 35.5 |
| Black | 9 | 50.0 | 531 | 45.4 |
| Hispanic | 4 | 22.2 | 220 | 18.8 |
| Sex | | | | |
| Male | 16 | 88.9 | 1,079 | 92.3 |
| Female | 2 | 11.1 | 90 | 7.7 |
| Diagnosis[a] | | | | |
| Axis I | | | | |
| Schizophrenia[b] | 14[c] | 77.8 | 520 | 45.5 |
| Schizoaffective disorder | 1 | 5.6 | 96 | 8.4 |
| Atypical psychosis | 2 | 11.1 | 24 | 2.1 |
| Organic mental disorder | 1 | 5.6 | 38 | 3.3 |
| Axis II | | | | |
| Antisocial personality disorder | 10 | 55.6 | 953 | 83.4 |
| Mixed personality disorder[d] | 2 | 11.1 | 58 | 5.1 |

[a] Percents of all patients are based on N=1,143 rather than 1,169. Diagnoses were not available for 26 patients.

[b] Difference between groups was significant ($\chi^2=6.31$, df=1, $p<0.05$).

[c] Two of these patients were presented to the court as having schizophreniform disorder; their symptoms were of more than 6 months' duration.

[d] Difference between groups was significant ($\chi^2=8.10$, df=1, $p<0.05$).

In accordance with the wording of the *Rivers* opinion, the psychiatrists for the hospital argued that 1) the patient was incompetent to make a treatment decision, 2) the patient would benefit from the proposed treatment, 3) the patient would be closely monitored for adverse side effects, especially tardive dyskinesia and neuroleptic malignant syndrome, and 4) there was no viable, less intrusive treatment. In addition, the hospital psychiatrists testified that without the proposed medication the patient posed some threat to his or her safety and/or that of others. The proposed treatment plans ranged from the very specific (e.g., 2 mg of haloperidol q.i.d. after meals) to the somewhat less specific (e.g., haloperidol on a sliding scale up to 60 mg/day). In no case did the psychiatrists recommend that the patient receive more than one psychotropic medication concomitantly. (It is the center's policy to review a patient's medication if a psychiatrist recommends the simultaneous use of two or more psychotropic medications.)

In each of the 15 *Rivers* hearings, the presiding judge ruled that the patient was incompetent to make a treatment decision and that the proposed treatment was "narrowly tailored to the patient's needs." With the exception of two cases, the order to proceed with treatment over the patient's objection remained in effect for the duration of the patient's involuntary commitment. In the other two cases, the judge's order was in effect for 90 days.

Ten psychiatrists from Central New York Psychiatric Center participated in the 18 *Rivers* cases. Of the ten, seven had had previous courtroom experience, and four of these were closely associated with the forensic fellowship program of the Department of Psychiatry at the State University of New York at Syracuse. On the average, each *Rivers* case required approximately 6 hours of a psychiatrist's time. In total, the first year of *Rivers* in practice at the Central New York Psychiatric Center demanded 108 hours of psychiatrists' time. Each of the psychiatrists interviewed expressed reservations about the interposition of court influence in treatment decision making and indicated that their physician-patient relationships were adversely affected by the interdiction of the court. They also implied that, when possible, they avoided bringing forced-medication issues to court. Some patients spent several weeks on the wards refusing medications before court action was considered. One psychiatrist stated that he arranged to be called when a patient refusing treatment became violent. In such instances, because the patient had been given emergency medications, the psychiatrist could then counsel the patient during what might be a rare lucid interval.

In each *Rivers* case, legal counsel for the patient was provided by Mental Health Legal Services and the hospital was represented by the district's attorney general. The same judge presided over the 15 hearings, which were held at the local county courthouse. In each *Rivers* hearing, the attorneys for both sides placed appreciable emphasis on the issues of the patient's competency to make a treatment decision and the appropriateness of the proposed treatment plan.

## DISCUSSION

Although the small number of patients involved in *Rivers* procedures precludes our drawing extensive statistically significant conclusions, certain demographic trends are apparent. Language barriers appeared to play no role in patient selection. Furthermore, race, sex, and educational level did not emerge as important factors in this respect. The only demographic data separating the *Rivers* group from the total psychiatric center population were age and diagnoses. The *Rivers* petition patients were older, and they had a higher rate of schizophrenic diagnoses. The latter finding suggests that patients with long-standing chronic schizophrenia are most affected by the *Rivers* decision, an observation that is consistent with reports from previous studies of patients who refuse medication (4, 5). That antisocial personality disorder was underrepresented is also consistent with the findings of other investigators of medication refusal and axis II diagnoses (6).

The issue of side effects and drug refusal has been widely studied, with contradictory reports that side effects may or may not be an important factor in psychiatric medication refusals (6–9). Of the 18 patients selected for *Rivers* petitions, 13 had refused the proposed medication because of denial of illness. None cited the adverse side effects of the antipsychotic drugs as the primary reason for refusal. All of the psychiatrists interviewed for this study expressed a desire to avoid a *Rivers* hearing, and to achieve this objective they entered into intensive counseling and negotiating with the patients. This intensive physician-patient contact may account for the relative absence of patients' claiming side effects as a primary reason for medication refusal, and it may also be seen as a benefit to the *Rivers* petition patients. It was, however, detrimental to the treatment of other patients on each psychiatrist's service. As one psychiatrist noted, "Sometimes I spend so much time with the *Rivers* patient that I do not have enough time to spend with the others."

The desire to avoid a *Rivers* hearing also affected the treatment of other medication-refusing patients. These patients, although not severely ill, remained in the hospital for weeks without the benefit of medications and without the initiation of formal *Rivers* procedures. In effect, their judgment and insight were not perceived as sufficiently impaired to deem them legally incompetent. Thus, for these patients, the hospital staff relied exclusively on less invasive treatment procedures, such as psychotherapy, occupational therapy, and recreational therapy. When these patients improved even slightly, they were discharged from the hospital and returned to the prison system.

The absence of any specific legal criteria defining competency to make a treatment decision with respect to antipsychotic medications provides the New York State psychiatrist with some latitude in determining which refusing patient should be taken to court for a legal ruling on competency (10–12). The fact that all the patients who had hearings during the first year of *Rivers* in practice were judged to be incompetent suggests that the psychiatrists' opinions on criteria for a determination of incompetency were accepted by the courts. The psychiatrists' testimony regarding the incompetency of the *Rivers* patients focused on three main arguments: 1) The patients' denial of their illnesses represented a gross lack of insight. 2) The patients' inability to recognize the benefits of the medication or the dangers of refusing treatment indicated severely disturbed judgment. 3) The patients were so delusional and disorganized that they could not make rational judgments about medication. These three criteria are essentially the same as those used by the Massachusetts psychiatrists in arguing their patients' incompetency under the *Rogers* law and are consistent with the opinions of forensic experts regarding criteria to determine competency (3, 12, 13).

When data from this study are compared with those from the Massachusetts experience with *Rogers*, striking differences emerge. In Massachusetts, all of the patients were found incompetent, compared with 90% of our patients. The *Rogers* patients took up 10.2 hours of a psychiatrist's time per case; the *Rivers* patients took 6.0 hours. In Massachusetts a larger proportion of patients (81.7/1,000 admissions) required forced-medication hearings than did our patients in New York (15.4/1,000 admissions). In addition, the hearings consumed much more time in Massachusetts under *Rogers* (mean=135 days, range=60–210 days) than they did in New York under *Rivers* (mean=24 days, range=8–53 days). What factors might account for these differences?

Although both the *Rogers* and *Rivers* decisions are based on similar constitutional and common law principles, these case laws have substantial philosophical and conceptual differences, as seen in the definition of competence, the protection of the patient's due process rights, the treatment evaluation process, and the method of implementing a forced-medication order.

Veliz and James (3) reported that Bridgewater State Hospital submitted 98 forced-medication petitions in the first year under the *Rogers* decision. They had projected, however, that if Bridgewater followed the *Rogers* decision precisely, 800 petitions would be submitted. These large numbers reflect the broad definition of incompetency in the Massachusetts law, which states that all patients in whom the competency question arises—not just those who refuse medication—should have a court hearing. The New York decision, however, defines incompetency in much more restricted terms, namely, that the opinion expressed by the court refers only to those patients who may be incompetent *and* who refuse medication. Thus, under *Rivers*, Central New York Psychiatric Center submitted forced-medication petitions at less than one-fifth the rate of that at the forensic psychiatric hospital in Massachusetts.

As expressed in the *Rogers* and *Rivers* decisions, the judicial differences between the two states with regard to the protection of patients' due process rights have led to two very different systems of evaluating treatment plans implementing these laws. The *Rogers* decision relies very heavily on the "substituted judgment" approach to due process protection. The philosophy of "substituted judgment" mandates that a guardian be appointed for the patient, which necessitates a court hearing. The *Rogers* study indicated that this procedure was responsible for some delays in implementing a forced-medication order. Once the guardian is appointed, it is the guardian's responsibility to try to predict what treatment the incompetent patient may have approved if he or she were competent, based on the recommendations of the psychiatrist. However, it is the judge's responsibility to approve a treatment plan and order its implementation. Since the psychiatrist must then seek approval from the guardian for any changes in the treatment plan, this procedural requirement involves appreciable additional time for the psychiatrist (3).

In contrast, New York's *Rivers* decision relies heavily on a "best interests" approach for the protection of the due process rights of the incompetent patient. Instead of appointing a guardian, the judge assumes the responsibility for the determination of what treatment is in the best interests of incompetent patients. We found that under *Rivers*, the local New York court determined that it was in the best interests of incompetent Central New York Psychiatric Center patients to place them in the care of the center's psychiatrists. These psychiatrists and the treatment plans had to be judicially approved. The New York courts have given considerable flexibility to the psychiatrists in determining the treatment plan, so it is unnecessary for them to seek approval for changes in medication if the protocol for such changes has been explained to the court at the *Rivers* hearing. Thus, each *Rivers* case required only one court appearance by the concerned parties, and follow-up time for the psychiatrist was minimal.

Finally, it is important to emphasize the effect of the participation of the forensic psychiatric fellowship program in these *Rivers* cases. All but two of the petitions were the primary responsibility of the fellowship program. The selection of patients for *Rivers* petitions and the subsequent presentations to the court were undoubtedly enhanced by the expertise offered through this program.

The difficulties and implications encountered in Massachusetts under the *Rogers* decision had been anticipated for the most part by forensic experts (9, 11, 14). The expense in terms of patient care, time, and money is enormous when compared with the procedure under *Rivers*. The concept of the patient's best interests seems to be a more efficient and inexpensive approach to the issue of how best to protect the patient's rights. Despite similarities between *Rivers* and *Rogers*, the latter remains the more protective right-to-refuse ruling but incurs a greater cost in terms of available resources.

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# Striatal $D_2$ Dopaminergic Receptors Assessed With Positron Emission Tomography and $[^{76}Br]$Bromospiperone in Untreated Schizophrenic Patients

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*Striatal $D_2$ dopaminergic receptors of 12 drug-free schizophrenic patients and 12 normal subjects were investigated with positron emission tomography and $[^{76}Br]$bromospiperone. Patients were classified according to* DSM-III *criteria, and their clinical symptoms were rated according to Andreasen's negative and positive symptom scales. The ratio of striatal to cerebellar radioactivity was taken as an index of striatal $D_2$ dopamine receptor density. There was no significant difference between the control subjects and the overall schizophrenic group and no significant relationship between this index and the symptom ratings. However, state-dependent variables could partly account for the striatal $D_2$ receptor density variability.*

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For the last decade, post-mortem studies of schizophrenic patients have showed higher than normal $D_2$ dopamine receptor density in the striatum (1). Although this finding could be explained by prior chronic neuroleptic treatment, which is known to increase the density of $D_2$ receptors in the striatum of laboratory animals (2), several studies (3, 4) have found these high densities in drug-free patients. In vivo studies of the striatal $D_2$ receptors using positron emission tomography (PET) have yielded conflicting results. Using $[^{11}C]$3-*N*-methylspiperone (NMSP), Wong et al. (5) initially found no abnormality of the NMSP striatum/cerebellum ratio in 13 chronic schizophrenic patients, but in a subsequent study (6) of 10 drug-naive and five previously treated schizophrenic patients, they found significant abnormalities that they interpreted as higher than normal $D_2$ receptor densities in the caudate nuclei. Farde et al. (7) used the highly specific $D_2$ antagonist $[^{11}C]$raclopride and found no significant abnormality in 15 drug-naive schizophrenic patients.

Those discrepant findings may be due to the use of different radioligands and/or a variability in $D_2$ receptor density related to clinical aspects of schizophrenia. For instance, it has been suggested (1) that there is a bimodal distribution in the density of $D_2$ receptors in schizophrenia, which would support the hypothesis that there are two forms of the disorder, separable both on the basis of behavioral or evolutive characteristics and on the basis of biological markers (8, 9).

The purpose of the present study was to compare the striatal $D_2$ receptors measured in schizophrenic patients and normal control subjects with another ligand, $[^{76}Br]$bromospiperone, and to search for a relationship between this measure and clinical data pertaining to the schizophrenic group.

## METHOD

### *Subjects*

Within a week of their admission, hospitalized patients were evaluated by psychiatrists (P.P.-M., V.C.) independent of the PET team. They observed and interviewed each patient, interviewed the patient's relatives and, in most cases, the physician who referred the patient, and examined the hospital report if one existed. Included in the study were consecutively admitted patients who fulfilled the following criteria: age over 18 years, male sex, *DSM-III* diagnosis of schizophrenic disorder, drug-naive or neuroleptic-free condition for at least 1 year and no history of chronic neuroleptic treatment, and clinical condition permitting the patient to wait without medication during the

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week necessary to determine whether the patient met the inclusion criteria, to administer the rating scales, and to evaluate the practicability of the PET study. Informed consent was obtained in all cases. The ethics committee of the Atomic Energy Commission approved the protocol of the study.

The subjects who met these criteria were 12 male schizophrenic patients (age range=21–52 years, mean±SD=28.7±8.7 years). Nine patients had never been treated with neuroleptics, and three had taken neuroleptics during a short period—less than 15 days—more than a year earlier and never since. None had taken benzodiazepines or antidepressants in the weeks preceding the study.

The clinical type and course of illness were classified for each patient according to *DSM-III* criteria. The distribution of types was as follows: paranoid, N=4; undifferentiated, N=4; and disorganized, N=4. The distribution of illness courses was subchronic, N=4; chronic with acute exacerbation, N=2; and chronic (without exacerbation), N=6.

### *Clinical Assessment*

For 10 patients, quantitative clinical evaluation was performed with the Comprehensive Psychopathological Rating Scale (10). The sum of the items was computed to estimate the severity of the global psychopathology. Those patients were also assessed with Andreasen's positive and negative symptom scales (11). Twelve scores were computed: the sum of the composite and global items in each subscale (five for negative symptoms, four for positive symptoms), the sum of the five negative symptom subscale scores and the sum of the four positive symptom subscale scores, and the ratio of these totals for negative and positive symptoms. This last index was to account for both the positive and negative dimensions, as each patient presented a combination of positive and negative symptoms.

The first two patients in this study were not assessed with those three rating scales; instead, they were evaluated with the Brief Psychiatric Rating Scale (BPRS).

The patients' ages, clinical types, illness courses, and test scores are presented in table 1.

The patient group was compared to a control group of 12 men individually matched for age (mean±SD=28.7±10.2 years) who were recruited from the hospital staff as the patients they matched were selected. Each control subject was screened by means of a physical examination and laboratory tests, conducted in the preventive medicine department, and an interview by a psychiatrist (J.-L.M., P.P.-M.). None used medications or had physical or mental problems.

### *PET Technique*

Bromospiperone labeled with bromine-76 (half-life=16.2 hours) was used to study the central dopaminergic $D_2$ receptors. Preparation of the radioligand and the method have been described elsewhere (12).

[$^{76}$Br]Bromospiperone was injected intravenously as a slow bolus. The injected mass ranged from 0.008 to 0.108 nmol/kg of body weight for the control subjects and from 0.008 to 0.090 nmol/kg for the patients (t=0.66, df=22, n.s., unpaired t test). The amount of radioactivity injected was 1.298±0.457 mCi for the control subjects and 1.346±0.333 for the patients (t=0.54, df=22, n.s., unpaired t test), with a specific activity of 0.935±0.583 nCi/ml for the control subjects and 1.212±0.812 for the patients (t=0.96, df=22, n.s., unpaired t test). The radiation absorbed by the liver is 1.5 rads for an intravenous injection of 1 mCi of [$^{76}$Br]bromospiperone.

The PET studies were performed with the LETI TTV01 time-of-flight positron camera, which provides seven simultaneous cerebral slices (axial resolution=13 mm; in plane resolution=13 mm) (13).

Each subject was examined at rest with eyes closed and ears unplugged. The subject's head was positioned in the head holder, by means of a crossed laser beam system, so that the lowest slice (10 mm above and parallel to the orbitomeatal plane) included the cerebellar hemispheres and the third slice (40 mm above the orbitomeatal plane) included the striata, according to two PET atlases (14, 15).

Before radioligand injection, a Ge-68/Ga-68 transmission scan was collected for subsequent attenuation correction. An early image was obtained between 0 and 15 minutes after the tracer injection. A second emission scan, lasting 30 minutes, began 4.5 hours after the injection. Accurate head repositioning was ensured by the projection of the external crossed laser beams on several ink marks drawn on the patient's face before the transmission scan. Whole blood radioactivity concentration was measured from a venous blood sample taken at the end of the second scan (mean ±SD radioactivity of this blood sample, expressed as fraction of injected dose per gram×$10^{-6}$, was [illegible].634±0.618 for the control subjects and 3.179±0.765 for the patients; t=1.58, df=21, n.s., unpaired t test).

The fraction of [$^{76}$Br]bromospiperone specifically bound to the $D_2$ striatal receptors was estimated by the striatum-cerebellum ratio obtained 4.5 hours after injection; the radioactive concentration in the cerebellum is a measure of nonspecific, or non-receptor-associated, tracer in the brain, while the striatal concentration reflects both specific and nonspecific binding. Therefore, the striatum-cerebellum radioactivity concentration ratio is a reliable index of the radioligand's specific binding in the striatum, which in turn reflects the status of the $D_2$ receptors under specified assumptions (12, 16).

### *Data Analysis*

In each case, the striatum and cerebellum were clearly visible on the late scan image (4.5 hours). The striatal radioactivity concentration (expressed as percent of injected dose per milliliter of brain) was automatically computed according to a standardized iso-

**TABLE 1. Clinical Data and Striatum-Cerebellum $D_2$ Dopamine Receptor Ratios of Untreated Schizophrenic Patients and Age-Matched Normal Subjects**

| | | | Positive Symptom Score | | Negative Symptom Score | | | |
|---|---|---|---|---|---|---|---|---|
| Subject | Age (years) | *DSM-III* Clinical Type | Sum of Composite Items | Sum of Global Items | Sum of Composite Items | Sum of Global Items | Global Psychopathology Rating[a] | Striatum-Cerebellum Ratio |
| Patients | | | | | | | | |
| Subchronic | | | | | | | | |
| 1 | 23 | Undifferentiated | 79 | 19 | 66 | 17 | 61 | 2.24 |
| 2 | 21 | Disorganized | 18 | 6 | 33 | 11 | 37 | 2.49 |
| 3 | 27 | Disorganized | 3 | 2 | 72 | 19 | 35 | 2.25 |
| 4 | 22 | Disorganized | — | — | — | — | 57 | 2.64 |
| Chronic with acute exacerbation | | | | | | | | |
| 5 | 35 | Undifferentiated | 29 | 10 | 42 | 10 | 39 | 2.32 |
| 6 | 22 | Paranoid | — | — | — | — | 52 | 2.08 |
| Chronic without exacerbation | | | | | | | | |
| 7 | 52 | Paranoid | 19 | 10 | 4 | 1 | 33 | 1.94 |
| 8 | 28 | Paranoid | 34 | 10 | 33 | 11 | 23 | 1.99 |
| 9 | 28 | Paranoid | 70 | 17 | 67 | 18 | 66 | 1.97 |
| 10 | 29 | Undifferentiated | 43 | 7 | 43 | 14 | 50 | 1.64 |
| 11 | 35 | Undifferentiated | 8 | 4 | 43 | 17 | 32 | 1.79 |
| 12 | 23 | Disorganized | 27 | 11 | 40 | 15 | 55 | 1.68 |
| Age-matched control subjects | | | | | | | | |
| 1 | 24 | — | — | — | — | — | — | 2.18 |
| 2 | 18 | — | — | — | — | — | — | 2.09 |
| 3 | 27 | — | — | — | — | — | — | 2.43 |
| 4 | 21 | — | — | — | — | — | — | 2.04 |
| 5 | 34 | — | — | — | — | — | — | 1.97 |
| 6 | 23 | — | — | — | — | — | — | 2.02 |
| 7 | 58 | — | — | — | — | — | — | 1.64 |
| 8 | 27 | — | — | — | — | — | — | 2.26 |
| 9 | 29 | — | — | — | — | — | — | 1.80 |
| 10 | 30 | — | — | — | — | — | — | 2.17 |
| 11 | 30 | — | — | — | — | — | — | 1.82 |
| 12 | 23 | — | — | — | — | — | — | 2.18 |

[a] Patients 4 and 6 were assessed with the Brief Psychiatric Rating Scale; all other patients were rated with the Comprehensive Psychopathological Rating Scale.

contour method that has previously been validated (17). The cerebellum radioactivity measurement was determined independently by two investigators unaware of the identities and diagnoses of the 24 individuals they were evaluating. Each cerebellar value was the mean of the radioactivity concentrations obtained from two regions of interest (area of each=6 $cm^2$), one in each cerebellar hemisphere.

The striatum-cerebellum ratios of the patients and age-matched control subjects were first compared by means of a paired t test. Three subsequent analyses involved the *DSM-III* classifications of clinical type and course of illness.

1. The three subgroups of patients with paranoid (N=4), undifferentiated (N=4), and disorganized (N=4) schizophrenia and the control group (N=12) were compared by means of a one-way analysis of variance (ANOVA). When the result of this test was significant, comparisons of pairs of subgroups were carried out by means of unpaired t tests with Bonferroni confidence levels for multiple group comparisons (18).
2. The subchronic (N=4) and chronic (N=8) patients were compared with each other and with the control group by means of the same statistical procedure.
3. We also used a diachronic perspective of the course of illness and divided the patients into those with recent onsets or relapses (N=6) (subchronic, N=4; chronic with acute exacerbation, N=2) and those with chronic schizophrenia without exacerbation (N=6). The same statistical procedure was used to compare these two subgroups to each other and to the control group.

Finally, we studied the correlations between the striatum-cerebellum ratio and the various rating scale scores for the schizophrenic group, using the Spearman rank correlation statistic. All statistical computations and tests were performed with the BMDP statistical package (19).

## RESULTS

For the 12 control subjects, the striatum/cerebellum radioactivity ratios ranged from 1.63 to 2.43 (mean±

SD=2.05±0.22); for the 12 patients, the ratios ranged from 1.64 to 2.64 (mean±SD=2.08±0.31). The mean values were not significantly different (t=0.93, df=11, p=0.37, paired t test). Individual values are shown in table 1.

For the control subjects, a significant linear correlation between the striatum/cerebellum ratio and age was found (r=−0.62, df=10, p=0.03; regression line of ratio with age: ratio=−0.013×age+2.428), whereas for the patients, the correlation coefficient was not significantly different from zero (r=−0.31, df=10, p=0.32); the slopes and intercept of the two groups were not significantly different.

We found no significant difference in striatum-cerebellum ratio between the control group and the subgroups based on *DSM-III* clinical types (F=0.7, df=3, 20, p=0.56).

Among the 10 patients rated with the Andreasen scales, most had mixed positive and negative symptoms. There was no significant correlation between the striatum-cerebellum ratio and the positive and negative rating score as represented by either the global evaluation items of the subscales or the sum of the composite and global items of each subscale. Moreover, the positive-negative symptom ratio varied independently of the striatum-cerebellum ratio. Likewise, the scores reflecting the severity of the overall symptoms (total of both positive and negative symptom scores and total score on the Comprehensive Psychopathological Rating Scale) did not correlate with the striatum-cerebellum ratio.

### *Course of Illness*

There was a significant difference in the mean striatum-cerebellum ratios of the three groups subchronic patients, chronic patients, and control subjects (F=6.65, df=2, 21, p=0.006). The four subchronic schizophrenic patients' ratio (mean±SD=2.41±0.19) was higher than the ratios of both the eight chronic schizophrenic patients (mean±SD=1.93±0.22; t=3.62, df=21, p<0.01) and the 12 control subjects (t=2.85, df=21, p<0.05). The mean ages of the three groups were not significantly different (control subjects: mean±SD=28.7±10.2 years, subchronic patients: 23.2±2.7 years, chronic patients: 31.5±9.5 years; F=1.05, df=2, 21, n.s.).

The difference between patients with subchronic or exacerbated chronic schizophrenia, chronic patients without exacerbation, and control subjects was also significant (F=9.65, df=2, 21, p=0.001). The mean ratio of the six patients with subchronic or chronic, exacerbated schizophrenia (mean±SD=2.34±0.20) was significantly higher than that of either the six chronic schizophrenic patients without exacerbation (1.83±0.15; t=4.36, df=21, p<0.001) or the 12 control subjects (2.05±0.22; t=2.88, df=21, p<0.05). The mean ages of these three groups were not significantly different (control subjects: mean±SD=28.7±10.2 years, subchronic or chronic with exacerbation: 25±5.3 years, chronic without exacerbation: 32.5±10.3 years; F=0.97, df=2, 21, n.s.).

### *Tracer Concentrations*

The cerebellar tracer concentrations were blindly determined by two independent investigators; the interobserver agreement was excellent (r=0.95, df=22, p<0.001, two-tailed significance levels of the correlation coefficient), and the mean absolute difference was less than 2%.

Fifteen minutes after injection, the cerebellar tracer concentrations (expressed as fraction of the injected dose×$10^{-5}$) of the control subjects and patients were not significantly different (mean±SD=1.07±0.26 and 0.97±0.12, respectively; t=1.12, df=20, p=0.27, unpaired t test). The mean early value of the four subchronic patients (0.96±0.10) did not differ significantly from that of the eight chronic patients (0.98±0.14) or the control subjects (F=0.6[illegible], df=2, 21, n.s.). Likewise, the mean early cerebellar value of the six patients who had chronic schizophrenia without exacerbation (1.02±0.09) was comparable to the values for the six patients with subchronic or chronic, exacerbated schizophrenia (0.93±0.16) and the control subjects (F=0.86, df=2, 19, n.s.).

The cerebellar values of the control subjects and patients were still similar at 4.5 hours (1.01±0.16 and 0.99±0.21, respectively; t=0.27, df=22, n.s., unpaired t test). The mean cerebellar value of the four subchronic patients (0.95±0.22) did not differ significantly from the values of the eight chronic patients (1.01±0.22) and the control subjects (F=0.[illegible]6, df=2, 21, n.s.). Also, the mean cerebellar value of the six patients with chronic schizophrenia without exacerbation (1.09±0.16) was comparable to the values of the six patients with subchronic or chronic, exacerbated schizophrenia (0.89±0.21) and the control subjects (F=1.89, df=2, 21, n.s.).

## DISCUSSION

The drug-free schizophrenic patients as a whole did not have a significantly higher $D_2$ striatal receptor density than the control subjects. Therefore, our data do not support the idea that a quantitative abnormality in a particular part of the dopaminergic system—the striatum—is systematically associated with schizophrenia.

This result concurs with that of Farde et al. ([illegible]), who used a highly selective $D_2$ ligand, [$^{11}$C]raclopride, and fails to confirm Wong et al.'s finding (6) of a 2.5 times higher $D_2$ receptor density in the basal ganglia of drug-naive schizophrenic patients than in control subjects. Those authors used not only different radioligands, but also different PET data analysis. Because they used $^{11}$C-labeled radioligands, their data collection was limited to 60 minutes after administration, rendering the measurement of the striatum-cerebellum ratio sensitive to the tracer's rate of access to the $D_2$ receptors (e.g., blood-brain barrier permeability, blood flow) (20). To minimize this problem, they developed models to measure $B_{max}$, the $D_2$ receptor density in striatum, assuming a number of underlying conditions. However, a series of differences between the Karolinska (Farde et al.) and Johns Hopkins (Wong et al.) studies have been identified (21) and could contribute to the divergent results. Also, Wong et al. (5) initially reported no abnormality in the striatum-cerebellum ratio of 13 chronic schizophrenic patients who had been without medication for an average of 7 months, a finding apparently consistent with our result.

Because of the relatively long half-life of bromine-76 (16.2 hours), our patients were allowed only a small radioactivity dose (less than 2 mCi), thus preventing us from collecting data at enough time points for adequate time-sequenced data modeling (20) and from performing a second PET study with the partial saturation necessary to measure $B_{max}$ and $K_d$ (22, 23). However, this very limitation of bromine-76 allows PET imaging to be delayed for 4.5 to 5 hours, thus permitting an essentially stable concentration of the radioligand in the striatum and cerebellum to be reached (12) and minimizing the influence of accessibility on the striatum-cerebellum ratio (17). In the present study it was impossible to obtain sequential PET scans to assess such stability of the radiotracer in brain tissues. Nevertheless, we found no difference between patients and control subjects in early tracer uptake in the cerebellum, suggesting similar accessibility. Furthermore, the lack of significant difference in the cerebellar concentration at 4.5 hours suggests similar nonspecific binding of bromospiperone to brain tissues.

Another technical point is the presence in the cerebellum of labeled metabolites of [$^{76}$Br]bromospiperone from the blood, which could interfere with PET measurement of the striatum-cerebellum ratio by contributing to the estimate of nonspecific binding. But biochemical blood studies performed on primates in our laboratory have shown that 4.5 hours after injection 15% of the blood radioactivity is related to lipophilic radioactive metabolite that is able to enter the brain. At this time, the blood-cerebellum radioactivity ratio is 0.25, and consequently, if we suppose an equilibration between blood and brain metabolite concentrations, the contribution made by the metabolite in the blood to the radioactivity of the cerebellum can be estimated at 4%. This figure appears to be an upper limit, because post-mortem biochemical brain studies performed with rats in our laboratory demonstrated that 4 hours after injection less than 2% of the radioactivity in the cerebellum was from lipophilic labeled metabolites. Although no information is presently available on the metabolism of bromospiperone in untreated schizophrenic patients, we found no difference between drug-free schizophrenic patients and normal subjects in the total radioactivity concentration in venous blood samples taken 4.5–5 hours after injection (see PET method), suggesting similar radioligand metabolism.

In spite of these considerations, the striatum-cerebellum ratio measured in our study is a density/affinity index of the striatal $D_2$ receptors, since this ratio has been found to decrease significantly in both normal aging (16) and progressive supranuclear palsy (17), and this decrease is of the same magnitude as the loss of $D_2$ receptors found in post-mortem examinations of subjects with these two conditions (24, 25). Also, the striatum-cerebellum [$^{76}$Br]bromospiperone ratio is reduced in a curvilinear dose-dependent mode in patients chronically treated with oral neuroleptics (26).

The lack of significant correlation between clinical type and either the rating scale scores or the striatum-cerebellum ratio may result from several factors. One is the small number of patients. Another factor is the clinical features of the patient sample: most patients had "mixed" schizophrenia, combining to various degrees positive and negative symptoms. However, the prevalence of purely positive-symptom or negative-symptom drug-naive schizophrenic patients is low, so such samples are difficult to constitute (27, 28). Of course, some findings do not support the dichotomy of distinct positive-symptom and negative-symptom forms of the disease (28–32).

In addition to these clinical issues, other limiting factors involve our method. The measurement of [$^{76}$Br]bromospiperone uptake allows only a global determination of striatal $D_2$ receptors. But striatal dopaminergic pathways are anatomically and functionally heterogeneous: human striata are organized in compartmentalized patches that are individualized within a matrix (33). There may be an intrinsic heterogeneity of dopamine function in the striata of schizophrenic patients that could be overlooked with the method used here. Moreover, it has been argued that the mesolimbic and mesocortical dopaminergic pathways are mainly affected in schizophrenia (34, 35), but PET studies are not presently suited to the investigation of these systems. Finally, two subtypes of dopaminergic receptors, the $D_1$ and $D_2$ types, coexist and interact in the striatum (36), and each type of receptor varies in its degree of affinity for dopamine (1). The ratio of $D_1$ to $D_2$ receptor activity may be important for interpretation of their functional effects (37).

The third finding of the study regards 1) the patients' illness duration—the mean striatum-cerebellum ratio was higher in subchronic patients than in either chronic patients or control subjects—and 2) the course of the symptoms—the group of subchronic patients and chronic patients with acute exacerbation had a higher mean ratio than either chronic patients without exacerbation or control subjects.

These findings related to the course of illness are ambiguous and must be considered with caution because of several methodological limitations. First, the very small number of subjects in the subgroups prevents us from drawing any definite conclusion. Second, the validity of distinguishing a subgroup including subchronic patients and chronic patients with exacerbation from a subgroup including chronic patients without exacerbation is questionable. It involves mixing and comparing subjects distinguished synchronically by means of criteria based on the time elapsed since the beginning of the illness (chronicity and subchronicity) and subjects diachronically distinguished on the basis of the course of the symptoms (presence or absence of exacerbation) in comparison to a previous stage. Likewise, the short duration of the subchronic patients' illness makes it difficult to distinguish between the course of their symptoms and the duration of their illness, since none of these patients had had time to improve to a residual phase. Nevertheless, the variability in the course of schizophrenia reported in prospective studies (38, 39) indicates a discontinuity of symptoms, i.e., recurrent acute episodes, in 50% to 70% of schizophrenic patients. This lack of symptom stability and the possibility of long-term improvement suggest that schizophrenia is not produced by a continuous process in all patients (40). Therefore, we pooled the patients whose symptoms had recently appeared or worsened (subchronic patients and chronic patients with exacerbation) and contrasted this group with the chronic patients without exacerbation, whose symptoms were stable. Obviously, an ideal study design should have included control patients with another diagnosis (e.g., bipolar with psychotic symptoms) and had a follow-up plan. Our findings related to the course of illness are therefore observations and must be taken as hypothesis-generating rather than established results.

The previously reported age-dependent decrease in $D_2$ striatal receptors (16, 25, 41) does not account for our findings related to the course of the illness, because the subchronic schizophrenic patients did not significantly differ from the chronic patients with respect to age and because the correlation between age and striatum-cerebellum ratio, which was significant for the control subjects, was not significant for the overall patient group. This intriguing absence of correlation in the schizophrenic patients is not explained by three patients' short neuroleptic treatment 1 year earlier, since the neuroleptic-induced $D_2$ increase (42) due to chronic neuroleptic treatment appears to last less than 6 months after treatment withdrawal (43, 44). Also, if those three patients are removed from the analysis, there is still no correlation between age and striatum-cerebellum ratio.

The fact that the subchronic patients had a higher ratio than the chronic patients could mean that this index diminishes with the duration of the illness, but this interpretation does not account for the even greater difference in mean ratio between the chronic patients without exacerbation and the patients experiencing recent emergence of symptoms or relapse regardless of illness duration.

These findings involving age and illness course would, however, be consistent with the hypothesis that dopaminergic system activity fluctuates as a function of state-dependent factors. Several indications indirectly support this hypothesis. There is evidence (45) that the level of CSF homovanillic acid is higher during acute phases of schizophrenia, reflecting greater activity in the dopamine systems of actively psychotic subjects. Although there is no study linking brain $D_2$ receptor density with dopamine activity in primates, apparent in vivo increases of [$^3$H]spiperone binding after increases in dopamine release have recently been demonstrated (46). Moreover, Wong et al. (47) recently pointed out increases of $D_2$ receptors related to active psychosis in manic-depressive illness.

In conclusion, the assessment of $D_2$ striatal receptors with [$^{76}$Br]bromospiperone suggests that the density of these receptors is not generally higher than normal in schizophrenia and is not related to qualitative aspects of the psychotic symptoms. However, the hypothesis of state-dependent fluctuations in the density of these receptors has to be considered.

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# Computer-Administered Cognitive-Behavioral Therapy for Depression

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*The authors evaluated a six-session interactive computer cognitive-behavioral treatment program given to volunteer patients who met Research Diagnostic Criteria (RDC) for major or minor depressive disorder. Patients were randomly assigned to computer-administered cognitive-behavioral treatment, to therapist-administered cognitive-behavioral treatment, or to a waiting-list control condition. After treatment and at 2-month follow-up, both treatment groups had improved significantly more than control subjects in their scores on the Beck Depression Inventory, SCL-90-R depression and global scales, Hamilton Rating Scale for Depression, and Automatic Thoughts Questionnaire. The treatment groups did not differ from each other at either time.*

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The purpose of this study was to carry out a randomized, controlled comparison of computer-administered cognitive-behavioral therapy with cognitive-behavioral treatment done by a therapist and with a waiting-list control condition. Despite the success of computer programs for patient assessment (1), early efforts to develop interactive programs for psychotherapeutic interactions have shown only that the general idea was feasible; they failed to go beyond limited demonstrations (2–4). A major obstacle to the development of clinically useful applications of computer-administered psychotherapy has been the difficulty of specifying and operationalizing therapeutic techniques and providing for the complexity of the therapeutic dialogue. This accounts for the fact that most applications to date have been for highly specific behavioral treatments (5, 6) or problem-solving protocols (7, 8), efforts that more recent reviews indicate are promising directions for the integration of computer applications into the treatment process (9, 10).

A major impetus toward solution of these problems has come from developments in behavioral and cognitive treatments for depression in which treatment is directed toward specific target behaviors and follows explicit steps with clearly defined goals and outcome criteria. For example, the procedures for cognitive-behavioral treatment as spelled out by Beck et al. (11), especially their didactic format, seem ideal for translation into computer-administered form. Although the efficacy of cognitive-behavioral treatment with a therapist is well established (12), this trial of a computer-administered form was designed to include two comparison groups, one in which the same procedures were administered by a therapist and the other a waiting-list control group. To make the treatment in both treated groups resemble clinical treatment as closely as possible, steps were taken to ensure that patients recruited from the community had clinically significant levels of depression. Finally, assessment extended 2 months beyond the end of treatment to determine the durability of treatment effects. Our hypothesis was that both treatment groups (computer- and therapist-administered) would show clinically meaningful reductions in depressive symptoms and dysfunctional cognitions but that waiting-list control subjects would remain unimproved.

## METHOD

Thirty-six patients were recruited by using newspaper announcements that included a questionnaire containing 13 depression items from the SCL-90-R (13) and additional items to exclude psychosis. Volunteers had to have depression scores on the SCL-90-R at or above the 65th percentile for psychiatric outpatients. Other inclusion criteria were Beck Depression Inventory (14) scores of 16 or above and current Research Diagnostic Criteria (RDC) (15) diagnoses of major, minor, or intermittent depressive disorder based on a modified version of the Schedule for Affective Disorders and Schizophrenia (SADS) (16). Of the 36 patients selected, the duration of the current depressive episode was up to 6 months for 18 patients, 6

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**TABLE 1. Characteristics of Patients Given Computer-Administered or Therapist-Administered Cognitive-Behavioral Therapy or No Therapy (Control Group)**

| Item | Computer-Administered Therapy (N=12) | Therapist-Administered Therapy (N=12) | Control Group (N=12) | Total (N=36) |
|---|---|---|---|---|
| Sex | | | | |
| Male | 5 | 4 | 4 | 13 |
| Female | 7 | 8 | 8 | 23 |
| Marital status | | | | |
| Single | 7 | 10 | 8 | 25 |
| Married | 3 | 2 | 4 | 9 |
| Divorced or separated | 2 | 0 | 0 | 2 |
| Education | | | | |
| Some college | 4 | 5 | 4 | 13 |
| College graduate | 2 | 5 | 6 | 13 |
| Graduate work or degree | 6 | 2 | 2 | 10 |
| Employment | | | | |
| Does not work | 3 | 1 | 3 | 7 |
| Works full-time or part-time | 3 | 5 | 6 | 14 |
| Is a student | 6 | 6 | 3 | 15 |
| RDC diagnosis during current episode | | | | |
| Major depressive disorder | 7 | 8 | 10 | 25 |
| Minor depressive disorder | 1 | 3 | 0 | 4 |
| Intermittent depressive disorder | 4 | 1 | 2 | 7 |

months to 3 years for 10, and more than 3 years for eight. Twenty-eight of the subjects were classified as chronically depressed, seven had from two to nine episodes of intermittent depression, and only one was experiencing a first episode. Twenty-seven had had previous psychotherapy.

Beck inventory scores at screening ranged from 16 to 35 (mean±SD=22.5±5.32); scores for 13 patients fell between 16 and 20, scores for 16 were between 21 and 26, and scores for seven were at or above 27. Scores on the Hamilton Rating Scale for Depression (17) at screening ranged from 7 to 23 (mean±SD=15.11±4.40); scores for 16 patients were 13 or below, and scores for 20 patients were 14 or above. Table 1 presents demographic characteristics of the patient sample. The mean±SD age of the patients in computer-administered cognitive-behavioral treatment was 28.9±4.89 and that of the patients given therapist-administered cognitive-behavioral treatment was 24.7±4.33; and that of the patients in the waiting-list control group was 30.9±3.88. The mean±age of the total sample was 28.2±4.58. All were nonminorities.

The cognitive-behavioral treatment program was designed by one of us (P.M.S.), who was trained in cognitive-behavioral treatment. The program was written in MIIS-CONVERSE (18) and run on a Data General Eclipse computer. In the first session, patients were taught to conduct the interview by a computer-administered teaching section that reviewed response formats and procedures for changing answers. Then the patient's experience with and expectations about computer interactions and reasons for seeking treatment were explored in open-ended questions such as, What do you expect from treatment? The Beck inventory, which would be administered at the beginning of each session to monitor any change in depression from week to week, was explained and administered. Next, the program assessed symptoms of depression and impairment in functioning. If a patient's problems were not listed, the program branched to free-text questions to personalize the remaining dialogue. The remainder of session one taught the key cognitive-behavioral treatment concept of automatic thoughts (ABC model) through exposition, graphic displays, and case examples. The patient then gave a personal example, specifying the event, feelings, and thoughts associated with the feelings. The program checked the patient's understanding of the material at several points and gave appropriate feedback. Finally, the program prepared a homework assignment for the patient to complete for the second session. Patients were given a short reading assignment and asked to keep a weekly record of their activities and feelings. The program provided a rationale for the assignment and gave explicit instructions for its completion.

Sessions two through six followed basically the same format, which included agenda setting, the Beck inventory, comparison of current and past weeks' Beck inventory scores, presentation of the patient's problems from the computer's memory (with options for redefinition), and verification of homework completion. If homework was not completed, the program explored attitudes and thoughts about treatment. Other concepts integral to cognitive-behavioral treatment were presented, such as continuing discussion of the relationship between automatic thoughts and feelings, increasing mastery and pleasure in daily activities, techniques to control automatic thoughts, and the role of underlying beliefs in depression. Teaching text was augmented by tests, exercises, and role plays to ensure comprehension.

Specific homework assignments depended on the program's assessment of the patient's reported activities during the previous week and could include keeping a daily record of dysfunctional thoughts (11), scheduling activities with high mastery and pleasure ratings (19), or a graded task assignment (20). The didactic portion of the program was augmented by recommended readings. Sessions flowed smoothly from one to the next, and the computer "remembered" each session and made comparisons between later sessions.

The therapist for the therapist-administered cognitive-behavioral treatment (S.P.S.) was an advanced graduate student in clinical psychology who received the same training in cognitive-behavioral treatment as the author of the cognitive-behavioral treatment program. For six sessions, he followed a treatment manual and session agendas that were identical to the computer program.

The waiting-list control subjects were told that they could begin treatment after 14 weeks and could call for an appointment in the interval if needed. No control subjects requested treatment during the waiting period; all but two control subjects requested and received treatment after the last follow-up.

At the initial screening by an independent interviewer (P.M.S. or S.P.S.), SADS and Hamilton depression scale ratings were made. Informed consent and randomization procedures were administered. Each patient then completed the Beck inventory and was given an SCL-90-R and an Automatic Thoughts Questionnaire (21) to complete at home. For subsequent Beck inventories, patients in treatment completed forms at their sessions and control subjects returned Beck inventories by mail each week. Also, at the end of each treatment session patients completed a 31-item checklist to describe session content and their reactions to each session. Items covered specific cognitive-behavioral treatment activities (e.g., "Discussed unreasonable thoughts") and more general nonspecific aspects of therapy (e.g., "Got insight into my problems"). At termination of therapy and follow-up the Hamilton depression scale was administered by the independent interviewer, who was blind to the patient's treatment and status on other outcome measures. In weeks 2–6 of the waiting period, the experimenter (P.M.S.) contacted each control subject by telephone to assess level of depression and suicide risk. Only on one occasion was this brief conversation extended to 20 minutes. Follow-up measures were administered to all treatment and control patients 2 months after treatment ended.

Both treatment conditions consisted of six sessions over 6 weeks. This interval was determined by the nature of the computer program. In the computer condition the patients had only minimal contact with the experimenter, who helped start and end the sessions and, although not in the room while the patient was interacting with the computer, was available to answer questions. Most questions had to do with computer procedures, and contact was kept to a minimum. There were no dropouts from any of the three groups during treatment.

## RESULTS

### *Depression, Total Symptoms, and Cognitive Change*

A multiple analysis of variance (MANOVA) of pretreatment depression scores (Beck inventory, Hamilton depression scale, depression scores on the SCL-90-R) showed no significant differences between the groups (F=0.21, df=6, 62, p<0.97). Treatment effects were examined in multiple analyses of covariance (MANCOVAs) of posttreatment and follow-up scores, with pretreatment levels as covariates. The overall group effect after treatment was significant (F=5.86, df=6, 56, p<0.0001). Univariate group effects were significant for Beck inventory scores (F=4.79, df=2, 30, p<0.01) and Hamilton depression scale scores (F=23.42, df=2, 30, p<0.0001) but not for the depression scores on the SCL-90-R (F=2.57, df=2, 30, p<0.09). For follow-up assessments, the overall group effect was significant (F=5.09, df=6, 54, p<0.0003), and univariate group effects were significant for each of the three depression measures (Beck inventory, F=11.68, df=2, 29, p<0.0002; Hamilton depression scale, F=17.70, df=2, 29, p<0.0001; depression scores on the SCL-90-R, F=7.44, df=2, 29, p<0.0025). Post hoc comparisons (Newman-Keuls, alpha=0.05), summarized in table 2, showed that both treatment groups were significantly more improved at both points than waiting-list control subjects.

Since the Beck inventory was given weekly throughout the active treatment period, it was possible to make a finer-grained assessment of change (see figure 1). A repeated measures analysis of covariance (ANCOVA) of Beck inventory scores, with initial Beck inventory scores as the covariate, yielded significant Time (F=8.16, df=7, 224, p<0.0001), Group (F=3.94, df=2, 31, p<0.03), and Time by Group (F=3.34, df=14, 224, p<0.001) effects. Post hoc analyses of simple effects indicated that group differences were significant at week 6 (F=4.55, df=2, 31, p<0.02), after treatment (F=4.66, df=2, 31, p<0.02), and at follow-up (F=12.51, df=2, 31, p<0.0001). Comparisons of group means showed that both treated groups had lower Beck inventory scores than did control subjects. There were no differences between the two treatment conditions on any of the depression measures. Effect sizes (22) for the depression measures based on control group means and standard deviations averaged −1.18 and −1.37 for the computer-administered therapy group and −0.99 and −1.26 for the therapist-administered therapy group at the two assessments.

Using Beck inventory scores of 9 or less to define clinical improvement, we found that six (50%) of the computer-administered therapy group and five (42%) of the therapist-administered therapy group were improved after treatment, compared with two (17%) of the control subjects. At follow-up, the differences were even greater—eight (67%) and nine (82% of 11 patients) in the computer and therapist groups, respec-

**TABLE 2. Scores on Measures of Depression, Global Symptoms, and Automatic Thoughts Before and After Treatment of Patients Given Computer-Administered or Therapist-Administered Cognitive-Behavioral Therapy or No Therapy (Control Group)**

| | Before Treatment | | After Treatment | | Effect Size[a] | Follow-Up | | Effect Size[a] |
|---|---|---|---|---|---|---|---|---|
| Variable | Mean | SD | Mean | SD | | Mean | SD | |
| Beck Depression Inventory[b] | | | | | | | | |
| Computer-administered therapy (N=12) | 21.42 | 3.96 | 10.33 | 5.18 | −0.88 | 6.17 | 5.57 | −1.47 |
| Therapist-administered therapy (N=12) | 23.18 | 7.19 | 11.64 | 8.20 | −0.74 | 8.27 | 8.84 | −1.25 |
| Control group (N=12) | 22.92 | 5.02 | 18.50 | 9.32 | | 20.67 | 9.89 | |
| Hamilton Rating Scale for Depression[b] | | | | | | | | |
| Computer-administered therapy (N=12) | 14.33 | 4.01 | 5.83 | 2.62 | −1.96 | 4.92 | 2.31 | −1.42 |
| Therapist-administered therapy (N=12) | 15.09 | 4.55 | 6.36 | 4.08 | −1.58 | 4.54 | 2.66 | −1.47 |
| Control group (N=12) | 15.57 | 5.00 | 13.83 | 4.74 | | 14.50 | 6.76 | |
| SCL-90-R depression scale[c] | | | | | | | | |
| Computer-administered therapy (N=12) | 1.76 | 0.61 | 1.11 | 0.72 | −0.71 | 0.73 | 0.57 | −1.21 |
| Therapist-administered therapy (N=12) | 1.91 | 0.63 | 1.16 | 0.54 | −0.64 | 0.89 | 0.80 | −1.05 |
| Control group (N=12) | 1.98 | 0.55 | 1.65 | 0.76 | | 1.92 | 0.98 | |
| SCL-90-R global symptoms scale[c] | | | | | | | | |
| Computer-administered therapy (N=12) | 1.10 | 0.31 | 0.67 | 0.38 | −0.45 | 0.49 | 0.31 | −1.11 |
| Therapist-administered therapy (N=12) | 1.02 | 0.48 | 0.66 | 0.33 | −0.43 | 0.53 | 0.48 | −1.02 |
| Control group (N=12) | 1.03 | 0.34 | 0.85 | 0.40 | | 0.98 | 0.44 | |
| Automatic Thoughts Questionnaire[b] | | | | | | | | |
| Computer-administered therapy (N=12) | 78.75 | 20.27 | 54.33 | 18.03 | −0.91 | 49.08 | 16.72 | −1.20 |
| Therapist-administered therapy (N=12) | 90.73 | 25.20 | 62.73 | 23.53 | −0.65 | 50.64 | 19.95 | −1.15 |
| Control group (N=12) | 82.08 | 17.30 | 84.17 | 32.73 | | 85.33 | 30.23 | |

[a] Effect sizes based on control group means and standard deviations after treatment or at follow-up.

[b] The scores of the two groups given therapy were significantly different at posttreatment and follow-up from those of the control group ($p<0.05$, Newman-Keuls).

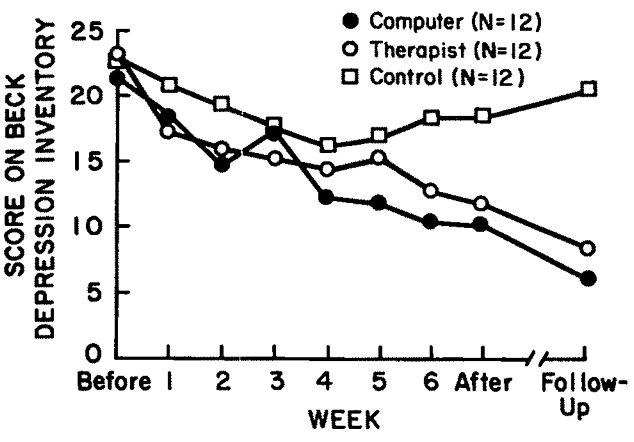
[c] The scores of the two groups given therapy were significantly different at follow-up from those of the control group ($p<0.05$, Newman-Keuls).

tively, versus one (8%) of the control subjects. Using a Hamilton depression scale cutoff of 6 or less to define improvement, rates after treatment and at follow-up were 50% (N=6) and 75% (N=9) for the computer group and 58% (N=7) and 73% (N=8) for the therapist group, compared with 8% (N=1) for the control subjects at both points.

There were no group differences for pretreatment global symptom scores on the SCL-90-R (F=0.025, df=2, 32, $p<0.80$). A repeated measures ANCOVA of posttreatment and follow-up global symptom SCL-90-R scores, with pretreatment global symptom scores as covariate, yielded a significant group effect (F=6.66, df=2, 31, $p<0.004$). As shown in table 2, the two treatment groups had significantly fewer symptoms than control subjects at both points.

There were also no significant differences in Automatic Thoughts Questionnaire scores at pretreatment (F=0.699, df=2, 33, $p<0.50$), but both treatment groups had significantly lower Automatic Thoughts

**FIGURE 1. Mean Weekly Beck Inventory Scores of Patients Given Computer-Administered or Therapist-Administered Cognitive-Behavioral Therapy or No Therapy (Control Group)**[a]



[a] There were only 11 patients in the therapist-administered therapy group at follow-up.

Questionnaire scores after treatment and at follow-up (repeated measures ANCOVA) than control subjects (group $F=11.75$, $df=2, 31$, $p<0.0002$) (see table 2). Because Automatic Thoughts Questionnaire and Beck inventory scores were correlated at each time point, we used ANCOVAs to consider the direction and magnitude of their effects on the changes found. When Automatic Thoughts Questionnaire scores were controlled as covariates in an analysis of Beck inventory scores, the Time effect ($F=20.93$, $df=2, 63$, $p<0.0001$) remained significant and the Time by Group interaction ($F=2.32$, $df=4, 63$, $p<0.07$) was near significance. When Beck inventory scores were used as covariates in analysis of Automatic Thoughts Questionnaire scores, the previously observed significant Time effect and Time by Group interaction did not hold (Time, $F=0.45$, $df=2, 63$, $p<0.62$; Time by Group, $F=1.76$, $df=4, 63$, $p<0.16$).

### *Patient Session Ratings*

Comparisons of patient session ratings using MANOVA for four scaled items and Fisher's exact test for 27 checklist items for each of the six treatment sessions yielded only three significant group differences out of 162 comparisons. In the first session, more patients in the therapist condition ($N=10$) than in the computer condition ($N=3$) checked having been exposed to "techniques for defining and solving my everyday problems" ($p<0.01$, Fisher exact test), and more therapist-treated patients ($N=11$) than computer-treated patients ($N=5$) perceived "therapist understanding" ($p<0.05$, Fisher exact test). In session six, more patients treated by the therapist ($N=8$) than computer patients ($N=3$) said they had learned "methods for dealing with people" ($p<0.05$, Fisher exact test). In general, the same six items were endorsed by the majority of patients for most sessions.

## DISCUSSION

Results indicate that this computer cognitive-behavioral treatment program was as effective in the treatment of mild to moderately depressed outpatients as a therapist using the same cognitive-behavioral treatment protocol. Although patients were recruited, most met RDC for major depressive disorder and all but one had repeated episodes, suggesting that these volunteers were comparable to actual patients (23). On all measures there were significant differences favoring cognitive-behavioral treatment, however administered, over the waiting-list control condition. Although the length of treatment was less than usually recommended for cognitive-behavioral treatment, improvement was substantial and equally durable for both treated groups. Effect sizes for most measures compare very favorably to those reported for meta-analyses of psychotherapy in general and cognitive-behavioral treatment in particular (24). Further, when norms for nondistressed control subjects or the general population are used for comparison, the average posttreatment effect sizes for the two treatment groups are 1.02 (Beck inventory compared with nondistressed control subjects) and 0.297, 1.415, and 0.85 (Beck inventory, depression scores on the SCL-90-R, and global symptom scores on the SCL-90-R compared with the general population). These are close to the averages of 1.62 (nondistressed control subjects) and 0.71 (general population) reported by Nietzel et al. (25) for 31 studies

In both forms of cognitive-behavioral treatment, changes in both automatic thoughts and depressive symptoms were found. Although the theory on which cognitive-behavioral treatment is based holds that the modification of cognitions is a necessary and/or sufficient condition of improvement in symptoms, our results did not fully support this view. Covariance analyses suggested, instead, that the cognitive-behavioral treatments influenced automatic thoughts only indirectly through their effects on depression. This is consistent with studies in which cognitive changes were found to accompany but not necessarily to precede improvement in symptoms (26–28).

Unfortunately, the nature of the computer sessions precluded audiotaped implementation checks. However, patients' ratings of the sessions showed differences in perceptions for the first and last sessions on only three of 31 items, and most of the ratings of session activities were consistent with cognitive-behavioral treatment agendas and procedures for both conditions. This, coupled with the significant and lasting improvement in depressive symptoms and attitudes, suggests that cognitive-behavioral treatment was implemented as intended in both active treatment conditions.

The novelty of the computer method may have influenced results with this group of predominantly computer-naive patients. The computer treatment group had some additional contact with the experimenter (about 20 minutes/week) for assessments. The stability of benefit beyond the 2-month follow-up period is unknown. One must be cautious in generalizing from the findings obtained with this sample of well-educated patients. It is uncertain whether similar results would be found with another population of depressed patients who might be less educated and/or more conservative, or more severely depressed or distressed.

No treatment can be administered free from nonspecific factors such as attention, expectation of success (29), or relationship variables such as "understanding, respect, interest, encouragement, acceptance, forgiveness and human qualities" (30). Although computer treatment programs could make it easier to study mechanisms of change by controlling for nonspecific factors, the present study did not address these issues.

In spite of the limitations of the present study and the role that nonspecific factors may have played in the results obtained, the computer cognitive-behavioral treatment program as used appears to be as effective as a human therapist in relieving mild to moderate depression. Although we want to emphasize that computer treatments must be used in the context of careful professional assessment and comprehensive management of patient problems, they may have a role to play in providing parts of effective, efficient, and economical treatment. Further development of direct patient-computer treatment programs, subject to rigorous evaluations, is warranted. Implementation of such programs in clinical settings should await the results of further research.

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# Cognitive Features of Borderline Personality Disorder

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*Of 50 patients with borderline personality disorder, 100% reported disturbed but nonpsychotic thought, 40% (N=20) reported quasi-psychotic thought, and none reported true psychotic thought during the past 2 years; only 14% (N=7) reported ever experiencing true psychotic thought. Disturbed and quasi-psychotic thought was significantly more common among these patients than among patients with other axis II disorders or schizophrenia and normal control subjects; however, true psychotic thought was significantly more common among schizophrenic patients. While disturbed thought was also common among axis II disorder and schizophrenic patients, quasi-psychotic thought was reported by only one of these subjects, suggesting that quasi-psychotic thought may be a marker for borderline personality disorder.*

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Stern (1) first introduced the term "borderline" 50 years ago to describe patients who he thought manifested both neurotic and psychotic symptoms. Since that time, psychoanalytically oriented authors such as Knight (2), Frosch (3), Kernberg (4), and Gunderson (5) have suggested that the tendency of borderline patients to develop psychotic or psychotic-like symptoms when sufficiently stressed is a core feature of the disorder. Despite the widespread clinical acceptance of this observation and the intense research interest in this aspect of the phenomenology of borderline personality disorder (6–30), the most characteristic and distinguishing cognitive features of the disorder are still unclear.

There are three main reasons for this lack of clarity. First, most studies have failed to systematically assess the full range of cognitive features of the disorder. Some studies (13, 22, 25, 26, 28, 29), for example, have focused on the prevalence of chronic eccentricities of thought associated with schizotypal personality disorder, while others (6, 7, 9–11) have focused on the prevalence of discrete psychotic episodes. Second, either formal comparison groups have not been used (6, 7, 24, 25) or they have usually been restricted to schizophrenic or depressed patients or general psychiatric control subjects (8–20, 22, 27). Perhaps most important, only four studies (16, 21, 26, 29) have made any effort to assess the cognitive distinctions between borderline personality disorder and a range of other *DSM-III* axis II disorders. Third, less than half of the studies (8, 13, 14, 21–26, 28–30) have presented the prevalence rates for each of the types of cognition they assessed. Most of the other studies (9–12, 15–20, 27) have presented mean scores or factor analytic results, which delineate between-group differences but shed little light on how characteristic each cognitive feature studied really is. In addition, interpretation of the results of most of these earlier studies has been hampered by the tendency to use the terms "psychotic" or "psychotic-like" to describe all cognitive difficulties—a definition of psychosis that is far more encompassing than the clear-cut departure from consensual reality described in *DSM-III*.

The current study built upon these earlier studies in four important ways. First, diagnostic assessments were made by using semistructured interviews based on rigorous research criteria. Second, patients with personality disorders, schizophrenic patients, and normal control subjects were studied. Third, we investigated all of the types of cognition described in earlier studies. Fourth, the three main levels of cognition that we explored—disturbed thought, quasi-psychotic thought, and true psychotic thought—were systematically assessed by using clearly delineated clusters of symptoms.

## METHOD

As part of a larger study of the validity of borderline personality disorder (31–34), 108 outpatients whose therapists felt that they met the *DSM-III* criteria for an axis II disorder had been recruited. Each of these patients was in treatment at one of three clinics in a metropolitan area. As part of an earlier study (35), two other groups of subjects had been recruited: 32 patients with definite clinical diagnoses of schizophrenia and 46 normal control subjects who had no history of serious psychiatric disturbance and who had no

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knowledge of the purpose of the current study. Half of the schizophrenic subjects were outpatients at one of the three clinics we have mentioned, and half were inpatients at a hospital in a neighboring community. All of the normal control subjects were employees of these four institutions.

All subjects gave written informed consent and were screened to determine that they 1) were between the ages of 18 and 40 years, 2) had normal or greater intelligence, and 3) had no history or current symptoms of an organic condition known to mimic or confound psychiatric symptoms. One of us (M.C.Z.), blind to the clinical diagnosis, then evaluated the diagnostic status of each patient with a personality disorder by administering three research instruments: 1) the Revised Diagnostic Interview for Borderlines (DIB-R) (36), a semistructured interview that can reliably distinguish clinically diagnosed borderline patients from those with other axis II disorders, 2) the Diagnostic Interview for Personality Disorders (37), a semistructured interview that reliably assesses the presence of the 11 axis II disorders described in *DSM-III*, and 3) the Structured Clinical Interview for DSM-III (SCID) (38), a structured interview for 20 of the most common *DSM-III* axis I disorders. The DIB-R and the SCID were also administered by the same rater, blind to clinical diagnosis, to each schizophrenic subject and in nonblind fashion to each normal control subject.

Of the 108 patients with axis II disorders, 50 met both the DIB and the *DSM-III* criteria for borderline personality disorder as assessed by the DIB-R and the Diagnostic Interview for Personality Disorders; they were included in the borderline group. Fifty-five others did not meet the study criteria for borderline personality disorder but did meet the *DSM-III* criteria for some other type of axis II disorder as assessed by the Diagnostic Interview for Personality Disorders; they were included in the other personality disorder group. The three remaining patients with axis II disorders were excluded from further study, two because they met the *DSM-III* criteria for a concomitant psychotic disorder and one who did not meet the *DSM-III* criteria for any axis II disorder as assessed by the Diagnostic Interview for Personality Disorders. All 32 schizophrenic patients met the *DSM-III* criteria for schizophrenia as assessed by the SCID. In addition, no schizophrenic or normal control subject met the study criteria for borderline personality disorder as assessed by our research instruments.

The cognitive status of each subject was evaluated by using two sets of items: 1) the cognition section of the DIB-R, which inquires about cognitive functioning in the past 2 years, and 2) the psychosis section of the SCID, which inquires about lifetime cognitive functioning. The cognition section of the DIB-R explicitly rates 27 types of cognition not associated with substance abuse. Twelve items are used to rate the presence of disturbed but nonpsychotic thought, and 15 items are used to rate the presence of psychotic thought. Only when disturbed thought is chronic or frequently recurring is it rated as present (e.g., the patient has had episodes of depersonalization off and on for most of the past 2 years). In addition, delusions and hallucinations that are judged to be transient (of less than 2 days' duration), circumscribed (affecting only one or two areas of the patient's life), or atypical of psychotic disorders (possibly reality-based or totally fantastic in content) are rated as quasi-psychotic experiences. In contrast, delusions and hallucinations that are judged to be prolonged (duration of 2 days or more), widespread (affecting many areas of the patient's life), or bizarre or stereotypic of psychotic disorders (Schneiderian first-rank symptoms or other gross departures from reality) are rated as true psychotic experiences.

The psychosis section of the SCID, which consists of 10 items that are also contained in the DIB-R, explicitly rates only true psychotic experiences. Each experience that was rated as a true psychotic episode was further rated as to whether it was related to substance abuse or depression or was of another functional nature (i.e., characteristic of a major psychotic disorder).

Between-group comparisons involving categorical data were computed using the chi-square statistic corrected for continuity (df=1 for all comparisons). Between-group comparisons involving continuous data were computed using analysis of variance. The Bonferroni correction for multiple comparisons was used where applicable.

## RESULTS

There were no significant differences in mean±SD age between the borderline subjects (29.2±6.4 years) and the other personality disorder (28.1±7.2), schizophrenic (26.2±5.4), and normal control (30.3±5.6) subjects. There was also no significant difference in the percentages of female subjects among the borderline subjects (66.0%, N=33) and the other personality disorder (54.5%, N=30), schizophrenic (50.0%, N=16), and normal control (65.2%, N=30) subjects.

Of the 55 subjects with other personality disorders, 36 (65.5%) met the criteria for a nonborderline "dramatic" cluster (histrionic, narcissistic, or antisocial) personality disorder, eight (14.5%) met the criteria for an "odd" cluster (paranoid, schizoid, or schizotypal) personality disorder, and 17 (30.9%) met the criteria for an "anxious" cluster (avoidant, dependent, compulsive, or passive-aggressive) personality disorder. (These percentages add to more than 100% because some subjects met the criteria for disorders in more than one cluster.)

Table 1 shows the percentage of those in each group who reported disturbed cognitive experiences. (Exact chi-square values for each of the comparisons in this and the subsequent tables can be obtained from the first author.) As shown in table 1, a significantly higher percentage of the borderline patients than of those in each of the other three groups reported experiencing

TABLE 1. Prevalence of Disturbed Thought During the Past 2 Years in 50 Patients With Borderline Personality Disorder and in Patient and Normal Control Subjects

| Cognitive Experience | Patients With Borderline Personality Disorder (N=50) | | Patients With Other Personality Disorders (N=55) | | Schizophrenic Patients (N=32) | | Normal Control Subjects (N=46) | | Significance of Difference (p)[a] | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | N | % | N | % | N | % | N | % | Borderline Versus Other Personality Disorders | Borderline Versus Schizophrenic | Borderline Versus Normal |
| Odd thinking | 34 | 68.0 | 13 | 23.6 | 6 | 18.8 | 1 | 2.2 | 0.0001 | 0.0001 | 0.0001 |
| Marked superstitiousness | 15 | 30.0 | 1 | 1.8 | 2 | 6.3 | 0 | 0.0 | 0.0002 | 0.02 | 0.0002 |
| Magical thinking | 17 | 34.0 | 5 | 9.1 | 3 | 9.4 | 0 | 0.0 | 0.004 | 0.02 | 0.0001 |
| Sixth sense | 15 | 30.0 | 5 | 9.1 | 3 | 9.4 | 0 | 0.0 | 0.01 | n.s. | 0.0002 |
| Telepathy | 7 | 14.0 | 3 | 5.5 | 2 | 6.3 | 0 | 0.0 | n.s. | n.s. | 0.02 |
| Clairvoyance | 6 | 12.0 | 2 | 3.6 | 3 | 9.4 | 1 | 2.2 | n.s. | n.s. | n.s. |
| Overvalued ideas | 7 | 14.0 | 3 | 5.5 | 1 | 3.1 | 0 | 0.0 | n.s. | n.s. | 0.02 |
| Unusual perceptions | 31 | 62.0 | 11 | 20.0 | 7 | 21.9 | 2 | 4.3 | 0.0001 | 0.0009 | 0.0001 |
| Recurrent illusions | 12 | 24.0 | 4 | 7.3 | 1 | 3.1 | 1 | 2.2 | 0.03 | 0.03 | 0.005 |
| Depersonalization | 18 | 36.0 | 8 | 14.6 | 3 | 9.4 | 0 | 0.0 | 0.02 | 0.01 | 0.0001 |
| Derealization | 15 | 30.0 | 5 | 9.1 | 6 | 18.8 | 1 | 2.2 | 0.01 | n.s. | 0.0007 |
| Nondelusional paranoia | 50 | 100.0 | 36 | 65.5 | 20 | 62.5 | 2 | 4.3 | 0.0001 | 0.0001 | 0.0001 |
| Undue suspiciousness | 46 | 92.0 | 33 | 60.0 | 17 | 53.1 | 1 | 2.2 | 0.0004 | 0.0001 | 0.0001 |
| Ideas of reference | 37 | 74.0 | 15 | 27.3 | 14 | 43.8 | 1 | 2.2 | 0.0001 | 0.01 | 0.0001 |
| Other paranoid ideation | 36 | 78.0 | 24 | 43.6 | 14 | 43.8 | 1 | 2.2 | 0.0007 | 0.003 | 0.0001 |
| Any disturbed thought | 50 | 100.0 | 39 | 70.9 | 21 | 65.6 | 3 | 6.5 | 0.0001 | 0.0001 | 0.0001 |

[a] Significance of difference was determined by 2×2 chi-square analysis. Application of the Bonferroni correction for multiple comparisons indicated statistical significance at $p<0.001$.

some type of disturbed cognition as well as each of the three main subtypes of disturbed thought: odd thinking, unusual perceptions, and nondelusional paranoia. The borderline subjects were also significantly more likely than the normal control subjects to have reported three of the six types of thought used to rate the presence of odd thinking (marked superstitiousness, magical thinking, and a sixth sense), two of the three types of thought used to rate the presence of unusual perceptions (depersonalization and derealization), and all three of the types of thought used to rate the presence of nondelusional paranoia (undue suspiciousness, ideas of reference, and other paranoid ideation). The borderline patients were significantly more likely than the subjects with other personality disorders to have reported one type of odd thought (marked superstitiousness) and all three types of nondelusional paranoia. In addition, they were significantly more likely than the schizophrenic subjects to have reported one type of nondelusional paranoia (undue suspiciousness).

The prevalence of psychotic thought is detailed in table 2. As can be seen, quasi-psychotic thought was almost pathognomonic for the borderline group and significantly distinguished them from each of the other groups. In addition, the percentages of borderline subjects reporting the main subtypes of this level of cognition (quasi-delusions and quasi-hallucinations) were significantly higher than those found in the other personality disorder and normal control subjects. In contrast, only the schizophrenic subjects were judged to have experienced true psychotic thought during the 2-year period assessed by the DIB-R. They reported a significantly higher prevalence of true psychotic thought and of the main subtypes of this level of cognition (true delusions and true hallucinations) than did the borderline subjects.

The lifetime prevalence of true psychotic episodes is shown in table 3. Only seven (14%) of the 50 borderline subjects had ever had a psychotic episode that lasted 2 days or more. Four of these subjects exhibited a concurrent major depressive episode, and the other three became psychotic after a period of substance abuse. Hallucinogens had recently been ingested in two of these cases, while the third was apparently the result of chronic amphetamine abuse. In contrast, 100% of the schizophrenic subjects reported having had a true psychotic episode, a prevalence significantly higher than that reported by the borderline subjects.

## DISCUSSION

### *Disturbed Thought*

One hundred percent of the borderline patients in this study reported experiencing disturbed but nonpsychotic thought; 100% reported nondelusional paranoid experiences, 68% reported some type of odd

**TABLE 2. Prevalence of Psychotic Thought During the Past 2 Years in 50 Patients With Borderline Personality Disorder and in Patient and Normal Control Subjects**

| | Patients With Borderline Personality Disorder (N=50) | | Patients With Other Personality Disorders (N=55) | | Schizophrenic Patients (N=32) | | Normal Control Subjects (N=46) | | Significance of Difference (p)[a] | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Cognitive Experience | N | % | N | % | N | % | N | % | Borderline Versus Other Personality Disorders | Borderline Versus Schizophrenic | Borderline Versus Normal |
| Quasi-psychotic thought | 20 | 40.0 | 1 | 1.8 | 0 | 0.0 | 0 | 0.0 | 0.0001 | 0.0001 | 0.0001 |
| Quasi-delusions | 10 | 20.0 | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 | 0.002 | 0.02 | 0.004 |
| Quasi-hallucinations | 13 | 26.0 | 1 | 1.8 | 0 | 0.0 | 0 | 0.0 | 0.0008 | 0.004 | 0.0006 |
| True psychotic thought | 0 | 0.0 | 0 | 0.0 | 31 | 96.9 | 0 | 0.0 | — | 0.0001 | — |
| Delusions | 0 | 0.0 | 0 | 0.0 | 28 | 87.5 | 0 | 0.0 | — | 0.0001 | — |
| Hallucinations | 0 | 0.0 | 0 | 0.0 | 22 | 68.8 | 0 | 0.0 | — | 0.0001 | — |

[a] Significance of difference was determined by 2×2 chi-square analysis. Application of the Bonferroni correction for multiple comparisons indicated statistical significance at $p<0.004$.

**TABLE 3. Lifetime Prevalence of Episodes of True Psychotic Thought in 50 Patients With Borderline Personality Disorder and in Patient and Normal Control Subjects**

| | Patients With Borderline Personality Disorder (N=50) | | Patients With Other Personality Disorders (N=55) | | Schizophrenic Patients (N=32) | | Normal Control Subjects (N=46) | | Significance of Difference (p)[a] | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| True Psychotic Thought | N | % | N | % | N | % | N | % | Borderline Versus Other Personality Disorders | Borderline Versus Schizophrenic | Borderline Versus Normal |
| Substance-related[b] | 3 | 6.0 | 2 | 3.6 | 0 | 0.0 | 0 | 0.0 | n.s. | n.s. | n.s. |
| Depression-related | 4 | 8.0 | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 | n.s. | n.s. | n.s. |
| Other functional | 0 | 0.0 | 0 | 0.0 | 32 | 100.0 | 0 | 0.0 | — | 0.0001 | — |
| Any episode | 7 | 14.0 | 2 | 3.6 | 32 | 100.0 | 0 | 0.0 | n.s. | 0.0001 | 0.02 |

[a] Significance of difference was determined by 2×2 chi-square analysis. Application of the Bonferroni correction for multiple comparisons indicated statistical significance at $p<0.005$.

[b] The following numbers of subjects in each group abused alcohol, marijuana, cocaine, or psychotomimetics: borderline patients, 41; patients with other personality disorders, 37; schizophrenic patients, 12; normal control subjects, 0.

thinking, and 62% reported at least one type of unusual perceptual experience. Disturbed thought was also commonly reported by the patients with schizophrenia and those with other axis II disorders but was almost never reported by the normal control subjects. However, borderline patients were significantly more likely to report having experienced this type of thought than those in any of the other groups.

The results of this study are consistent with the 38%–68% prevalence rate of odd thinking (13, 22, 25, 26, 29), the 30%–92% prevalence rate of unusual perceptual experiences (8, 13, 21, 24–26, 29, 30), and the 49%–77% prevalence rate of various forms of nondelusional paranoia (13, 22, 24–26, 29) found in earlier studies that used clinical or research interviews to assess the presence of these cognitive features. The results of this study are also consistent with those of earlier studies (11–19, 22, 27) which, taken together, found that the prevalence of each of these forms of thought was significantly higher in borderline subjects than in a variety of nonpsychotic and nonschizotypal control subjects. However, they contradict the results of earlier studies (8, 11, 12) which found that dissociative experiences were either significantly more common in schizophrenic patients than in borderline patients or about equally common. The reason for this difference is probably that the *DSM-III* criteria for schizophrenia used in the current study defined a more circumscribed, more chronically psychotic group of patients than those selected by the flexible system for diagnosing schizophrenia used in the earlier studies (39). Our results also contradict Pope et al.'s finding (23) that the prevalence of disturbed thought in borderline patients without histories of psychosis could not be distinguished from that of normal control subjects. This difference is due, at least in part, to the fact that the version of the DIB used in the present study includes a far more detailed and explicit assessment of disturbed forms of cognition than the version used in the Pope et al. study.

Taken together, these results suggest that disturbed thought is prevalent in many types of patients with serious psychopathology. This lack of specificity, in turn, suggests that the presence of disturbed thought is not in itself a particularly good marker for borderline personality disorder.

### *Quasi-Psychotic Thought*

Forty percent of the borderline patients in this study reported having quasi-psychotic experiences; quasi-hallucinations were somewhat more common than quasi-delusions (26% versus 20% of the borderline personality disorder sample). This type of thought was virtually pathognomonic for the borderline patients and successfully discriminated them from those in each of the other groups. Other studies have also found that this type of thought is both characteristic of (6, 8, 11, 12, 15, 18–20, 22–25) and highly discriminating for (12, 15, 18, 19, 22, 23) borderline patients. However, the results of this study contradict those of Frances et al. (21), who found "brief psychotic episodes" to be both relatively rare in borderline patients (11%) and about equally common in patients with other axis II disorders (8%). This discrepancy may be the result of methodological differences in assigning diagnoses and/or differences in the definition and assessment of this type of thought. In any case, our results extend the findings of many earlier studies which used axis I control subjects by suggesting that borderline patients are the only patients with axis II pathology who manifest a heightened prevalence of quasi-psychotic thought. In this regard, it is notable that none of the eight subjects with other axis II disorders who met the *DSM-III* criteria for an "odd" cluster disorder manifested this type of thought.

Taken together, the results of this study suggest that quasi-psychotic thought is a highly discriminating clinical feature of borderline personality disorder. This specificity, in turn, argues for the inclusion of quasi-psychotic thought in future sets of criteria for borderline personality disorder.

### *True Psychotic Thought*

Only 14% of the borderline patients in this study reported having had a true psychotic episode sometime during the course of their lives, and each of these episodes occurred in the presence of a concomitant axis I disorder. Those with other forms of personality disorder were about equally likely to have had a psychotic episode during their lifetimes. However, a significantly higher percentage of the schizophrenic subjects than of the borderline subjects reported experiencing such an episode. The far higher prevalence of true psychotic symptoms among schizophrenic than among borderline patients is consistent with the results of earlier studies (8, 11, 18, 19). The results of this study are also in keeping with Pope et al.'s finding (23) that the true psychotic episodes which borderline patients experience occur only in the context of either a concomitant substance use disorder or a concomitant affective disorder. However, they depart from the results of earlier studies (12, 18, 19) which found that substance-induced psychotic episodes were significantly more prevalent among borderline patients than among nonpsychotic control subjects; perhaps this is because in the present study the percentages of borderline subjects and subjects with other personality disorders who had histories of substance abuse were roughly equivalent (33), whereas in the earlier studies (12, 18, 19), such histories were significantly more common among the borderline subjects than among the mostly depressed control subjects with whom they were compared. Our results also extend the findings of these earlier studies by suggesting that borderline patients are not the only patients with personality disorder who experience prolonged psychotic episodes. Taken together, these results join those of most family history studies of criteria-defined borderline subjects (32, 40–48) to suggest that there is little, if any, relationship between borderline personality disorder and psychotic disorders, particularly schizophrenia.

Perhaps more discriminating than the three levels of thought taken separately is the overall cognitive pattern displayed by the borderline patients. Clearly, the pattern of ubiquitous disturbed thought, common quasi-psychotic thought, and rare true psychotic thought displayed by the borderline subjects is very different from the pattern of common disturbed thought, rare quasi-psychotic thought, and rare true psychotic thought displayed by those with other axis II disorders. It is also very different from the pattern of common disturbed thought, no quasi-psychotic thought, and ubiquitous true psychotic thought displayed by the schizophrenic patients and from the pattern of rare disturbed thought and no quasi-psychotic or true psychotic thought displayed by the normal control subjects.

The presence of a concomitant axis I disorder seems to explain the true psychotic episodes manifested by borderline patients. However, the etiology of both disturbed thought and quasi-psychotic thought remains unclear. The emergence of these kinds of thought might also be associated with the presence of a concomitant axis I disorder. This seems unlikely, however, as the occurrence of both types of thought was neither due to substance abuse nor limited to discrete episodes of other axis I disorders. Nevertheless, the possibility that their development is associated with the presence of some type of coexisting chronic and/or subacute axis I disorder cannot be ruled out.

In terms of other etiological explanations, some authors (2–5, 49, 50) have suggested that disturbed and quasi-psychotic thought develop in response to environmental stressors, particularly those of an interpersonal nature. Other authors (23, 51) have suggested that the primary motivation for these types of thought is the desire to assume or maintain the patient role. Still other authors (52, 53) have suggested that there is a strong association between the development of these types of thought and a childhood history of sexual trauma. Our clinical and research experience suggests that all three of these factors are common and often coexist in the same patient; each appears to predominate at different times in different patients.

Further outpatient studies are necessary to confirm the results of this study. Further studies are also necessary to determine whether these results are equally true for inpatients with borderline personality disorder. In addition, studies that assess the potentially different etiologies of disturbed thought and quasi-psychotic thought are needed. Finally, studies that attempt to assess the differential response of disturbed thought, quasi-psychotic thought, and true psychotic thought to various types of pharmacotherapy and various psychosocial interventions are needed.

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# Combined Alcoholics Anonymous and Professional Care for Addicted Physicians

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*The authors studied 100 impaired physicians who were successfully treated in a program that combined professionally directed psychotherapeutic treatment and peer-led self-help. An average of 33.4 months after admission they all reported being abstinent and rated Alcoholics Anonymous (AA) as more important to their recovery than professionally directed modalities. Feelings of affiliativeness to AA, which were very high, were strong predictors of the respondents' perceived support for their recovery. These feelings, and an identification with the role of care giver in addiction treatment, appeared to be central to their recovery process.*

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In the United States, psychiatric treatment for substance abuse has come to rely heavily on peer-led self-help programs, such as Alcoholics Anonymous (AA). There has, however, been relatively little controlled research on the way such modalities operate, given the large numbers of persons involved. There is also a notable paucity of investigations on the way such programs interact with medically directed psychotherapeutic care (1, 2). In order to clarify how peer-led and psychiatric modalities can be effectively integrated, we undertook a study of patients who had been rehabilitated in a treatment system that combined both approaches. We chose the Georgia Impaired Physicians Program because of its longstanding commitment to combining professional care with AA-based peer-led groups; its longitudinal model of rehabilitation from hospital, to halfway house, to aftercare; and its extensive experience, with more than 2,000 patients referred over 13 years from 49 states (3).

## METHOD

This study was designed to evaluate a cohort of physicians, alumni of the Impaired Physicians Program, who had elected to attend one of the annual retreats organized by the program's medical directors. Approximately 550 invitations were sent out to recent alumni of the program, and altogether 120 of the invitees attended. The staff of the program reported that the most common reasons given for not attending the retreats were insufficient time off from work, participation in a previous year's program, previous exposure to the scheduled speakers, conflicting medical conferences, and ill-health. In addition, some invitees were lost because of relocation without change of address or because of relapse to drug use.

Participation in the study itself was voluntary and anonymous, and participants were asked by the program director (D.T.) to respond as frankly as possible. It was further made clear that questionnaires would be collected and tabulated by an independent investigator (M.G.) and that only group data would be reported. By means of on-site administration, mailings, and follow-up calls, 116 of 120 participants at the retreat completed a research questionnaire. Of these, 16 were disqualified, one because of a primary diagnosis of bulimia and 15 because they were nonphysician health professionals. The remaining cohort of 100, whose responses are presented here, were recovering physician substance abusers who resided in 29 states and Canada.

The research instrument included 160 multiple-choice or numerical-response items, codable for computerized scoring. The research instrument included items that dealt with demography, professional activity, and drug abuse, as well as the 18-item General Well-Being Schedule, developed and standardized by the National Center for Health Statistics (4). Typical items on this schedule are "Have you been anxious, worried, or upset?" "Have you been waking up fresh and rested?" Responses are given on a 6-point scale. A comparison group (N=315), drawn from a national probability sample developed by Ware et al., was matched to the respondent group for age and sex (5).

Also included were attitudinal and self-assessment items, for which responses were made on a 5-point scale (1=not at all, 5=very much), as follows. Treat-

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ment components were rated for the degree to which they contributed to the respondent's own recovery. Respondents evaluated "the degree to which each of the following treatment components contributed to the process of your recovery after you entered the IPP [Impaired Physicians Program]"; they used target items that were developed for face validity, such as "physician counseling" and "family therapy." A cohesiveness scale had been used previously to assess other zealous groups (6, 7). It consisted of six items on which respondents rated the depth of their cohesive feelings toward the 10 12-step (AA and related groups) members they knew best and then toward the 10 nonmembers they knew best. Typical items are "They care for me" and "I care for them." (The internal consistency of the scale was found to be satisfactory in the aforesaid studies by computing the coefficient alpha, 0.86, for both the member and nonmember target groups.) An AA belief scale consisted of seven items that explicitly reflect commitment to the principles of the 12-step movement (with a coefficient alpha of 0.66 determined on this study population). Whenever possible, items were drawn explicitly from the AA wording of the 12 steps. Typical items are given in the section on results. A scale of four items was used to rate each of four sources of support for the actual assistance contributed to the respondent's own recovery; the sources of support were 12-step principles, fellow 12-step members, treating doctors, and family members (alpha coefficients were computed as 0.90, 0.82, 0.87, and 0.88, respectively, for this population). Results of the survey are for the entire sample of 100 respondents, unless otherwise indicated.

## RESULTS

### *Respondents' Background and Drug Use*

Most subjects were married (N=70), middle-aged (mean±SD age=46.3±9.7 years), and male (N=93). The areas of current specialty practice most frequently represented were addiction treatment (N=22), surgery (N=18), general and family practice (N=15), internal medicine (N=11), obstetrics (N=8), anesthesiology (N=7), and psychiatry (N=6). Fifty-seven respondents had been certified in a specialty recognized by the American Board of Medical Specialties.

Forty-four subjects reported alcohol as the principal drug problem, and all of them had drunk daily for at least 1 month before admission. Prescription opiates and analgesics, as a category, was designated as the greatest drug problem by 37 respondents; 22 of them had injected drugs intravenously, but only six had ever used heroin. Seven others reported that cocaine was their greatest drug problem.

Many of the respondents had used more than one drug. Those most frequently used for at least 1 month on a daily basis in the past by any respondents were, in rank order, alcohol (N=83), prescription opiates or analgesics (N=55), anxiolytics (N=37), stimulants (N=24), marijuana (N=22), other depressants (N=20), cocaine (N=13), heroin or illicit methadone (N=5), and psychotomimetics (N=2). One measure of the interference with function caused by respondents' additive problems was that an appreciable minority (N=37) had formal restraints placed on their medical practices due to substance abuse: Three had their licenses revoked, 15 had their licenses suspended, and 19 were placed under restrictive conditions.

### *Treatment Experience*

The standard format for treatment was a period of hospitalization followed by a halfway house program, and then outpatient status to follow-up. Respondents had entered the Impaired Physicians Program a mean ±SD of 33.4±32.9 months earlier and had spent an average of 4.1±1.6 weeks in the hospital, followed by 15.1±9.4 weeks in transitional residence, all within the program's treatment system. Aftercare included attending the Caduceus Club, a group for impaired physicians with an AA-like format, which served as a bridge to regular 12-step meetings (e.g., AA, Narcotics Anonymous, Drugs Anonymous). Respondents had attended 2.4±2.2 such meetings in the last month. After residential care, respondents also underwent observed urine sampling for varying periods of time. Fifty-two had had urinalyses within the last 3 months, an average of 5.1±5.8 times each.

Program participants were expected to attend 12-step meetings, and all but three indicated that they had gone to at least one meeting weekly during the past month; the average attendance was 5.5±4.6 meetings a week, which took up 10.4±8.5 hours. Of these meetings, the large majority (4.5±3.5) were AA; others were Drugs Anonymous, Cocaine Anonymous, and Narcotics Anonymous. Most respondents (N=7[illegible]) had also spoken with their AA sponsor during the last week.

The majority (N=54) of the cohort was also currently in some form of psychotherapy, with psychiatrists (N=13), other physicians (N=15), psychologists (N=19), or other professionals (N=26). These respondents spent an average of 1.23±0.75 hours in therapy weekly. Only four respondents were currently taking medications prescribed for psychiatric problems.

### *Outcome of Treatment*

Respondents' answers reflected a stable, drug-free adaptation. Only 14 indicated that they had used alcohol or drugs since entering the program, and of 66 who had been in the program more than a year, all but two reported at least a year's sobriety. None reported using any drugs of abuse within the last month. All but five were practicing medicine, and all but eight were treating patients. Overall, respondents spent an average of 38.4±17.8 hours weekly on patient care. Thirty-four had medical school faculty appointments (19 in professorial ranks), and two were residents. Their psychological General Well-Being Schedule rating was not significantly different from that of the sex- and age-matched sample (N=315) from the general population (83.0±12.1 versus 82.0±14.5) (7).

### *AA and Recovery*

AA was apparently perceived by respondents as the most potent element in their recovery. It ranked highest (on the 5-point scale) among treatment components contributing to the process of their recovery, with a mean score of 4.4±1.1, versus 3.3±1.1 for physician counseling, 3.3±1.3 for desire to do well at work, 2.9±1.4 for family therapy, and 1.9±1.1 for urinalyses (analysis of variance [ANOVA] for repeated measures: F=67.5, df=4, 396, $p<0.001$). In addition, responses to items on the AA belief scale reflected a considerable depth of commitment, with a mean score of 4.61±0.37 (maximum score=5). Thus, the large majority of respondents gave a rating of 4 or 5 to "The alcoholic is powerless over alcohol (N=99) (first AA step) and "The recovering substance abuser should carry the 12-step message to other addicted persons" (N=93).

The cohesiveness scales also reflected the intensity of affiliative feelings for fellow AA members. Mean scores for the "ten 12-step members you know best" (4.1± 0.60) were significantly higher than those for the "10 *non*members you know best" (3.2±0.70) (t=11.42, df=99, $p<0.001$, repeated measures), even though the latter group included friends and close associates. For example, 85 of the respondents gave the former group scores of 4 or 5 on "they care for me," whereas only 42 rated the latter group that highly. Indeed, mean cohesiveness scores for the 10 fellow members known the best were not significantly different from those given by members of a highly cohesive religious sect who espoused abstinence and lived and worked together communally (N=237; mean score=4.2±0.93) (5).

The scale measuring the actual assistance contributed toward respondents' recovery also reflected the importance of the AA role. Each source of support was evaluated for the aid it had provided the respondent in achieving a stable recovery. Mean scores on this scale for 12-step principles (17.5±3.1) and fellow 12-step members (17.2±2.8) were higher than those for the doctors who treated them (13.6±4.3) and for their own family members (12.0±4.6) (ANOVA for repeated measures: F=59.6, df=3, 291, $p<0.001$). Thus, the number of respondents who gave scores of 4 or 5 on the typical item "Helped me when I slipped [from abstinence], or might have" were, respectively, 84, 82, 43, and 41 for each support group just noted.

Intensity of commitment to AA was a significant predictor of perceived benefit. This was revealed in two stepwise multiple regression analyses in which respondents' scores for assistance contributed served as dependent variables. In both analyses predictors were entered into the regression equation as long as each accounted for a portion of the variance significant at the 5% level. In the first analysis, items reflecting AA beliefs predicted 43% of the variance in scores on respondents' assessment of the actual assistance contributed to their own recovery by 12-step principles. In the second analysis, items from the scale of cohesiveness toward the 10 12-step members they knew best predicted 26% of the variance in scores for actual assistance contributed from 12-step program members.

The evolution of the respondents' recovery careers is revealing, in that most initially relied more on receiving help from professional care givers and later on their own role of helping other addicts. This is evident in a number of ways. For most, the initial medically directed residential treatment was followed by professional ambulatory therapy early on after discharge, and then, therapy was generally terminated. Thus, those respondents who were currently in psychotherapy (N=54) had entered the program relatively recently (an average of only 24.0±29.8 months before). Those not in professional therapy (N=46), on the other hand, were generally at a later stage of recovery, having begun the program 44.4±33.3 months before (t=3.24, df=99, $p<0.01$).

Two aspects of the care giver role emerged with time: helping new AA members and serving as professionals in addiction treatment. Thus, those who served as sponsors in AA (N=43) had begun the Impaired Physicians Program 50.7±35.4 months before, whereas those who had not yet served (N=57) had begun only 20.3±23.8 months before (t=4.87, df=99, $p<0.001$). Furthermore, an examination of the medical practice of the respondents revealed a growing involvement in the addiction treatment field with time. Thus, 38 subjects reported that they were currently involved in some clinical work in addiction treatment programs, whereas only five had been doing such treatment before joining. Indeed, 22 subjects identified addiction as their primary specialty of medical practice, whereas only two had designated that specialty for the period before they joined the program.

Respondents' entry into addiction work later in the course of their recovery is further illustrated by those subjects who were involved in any addiction-related professional activities (treatment, clinical administration, teaching, or research). The 51 thus involved had joined 49.04±36.66 months before, whereas those not yet involved in addiction activities (N=48) were relatively new in their recovery careers, having joined only 17.31±17.34 months before (t=5.56, df=98, $p<0.001$). Indeed, fully 90% (N=27 of 30) of those who had entered the program at least 3 years before were now involved in doing professional work in the addictions.

These changing roles stand in contrast to respondents' AA attendance, which was stable over time. Neither the number of meetings attended nor the number of sponsor contacts was significantly correlated with time since admission to the program (r=0.01 in both cases). A representative case history follows.

## CASE REPORT

Dr. A, a 60-year-old married psychiatrist, was consuming one quart of 86-proof liquor and 650 mg of propoxyphene daily and had been hospitalized five times before for detoxification. He had been in psychotherapy for 2 years when he was hospitalized a sixth time, for alcoholic seizures. Upon discharge he relapsed to substance abuse within days, but a month later he applied for admission to the Impaired Physicians Program for the first time, on the recommendation of a physician friend and under pressure from his wife. He was admitted to the program's inpatient service for 1 month, where he attended AA meetings daily and underwent group, family, and vocational therapy, all couched in a daily 13-hour intensive therapeutic program. From there he was transferred to a 6-bed apartment to live with other recovering physicians, where he received daily counseling and participated in peer support (Caduceus) groups that focused on the AA steps toward recovery. After 1 month, in accordance with the standard treatment plan, he began counseling nonphysician patients at a local substance abuse program and also addressed students at a nearby medical school on the nature of addiction. All of this was discussed in peer counseling sessions designed to aid him in confronting his own denial.

Four months after admission to the program he was discharged from the halfway house apartment to live with his wife, and he elected to remain in the area and work in an addiction treatment facility, hoping to pursue accreditation as an addiction specialist in time. A year later he continued in this work, was still abstinent, and was attending five AA meetings and two peer-led Caduceus meetings weekly.

## DISCUSSION

Generalizations from these findings must be tempered because of the unusual nature of the respondents. Although similar in demographics and drug abuse to the full cohort of persons admitted to the Impaired Physicians Program (3), they represent, no doubt, a skewed outcome, since patients who had relapsed to drug use would be less likely to attend such a retreat. Conclusions about the efficacy of such a program must clearly await a prospective study on admissions to the Impaired Physicians Program, which is now under way (8), as well as studies of similar treatment formats for nonphysician populations. In addition, the attitudes toward treatment in the cohort evaluated in this study are not necessarily congruent with those of program alumni who did not attend the retreat. Those attending are more likely to be among the patients who adhere more closely to this value-laden treatment program. Furthermore, substance abuse self-reports during treatment are not always reliable because of the vulnerability to denial. In favor of correct responses, however, is the fact that these respondents participated voluntarily and anonymously, and they were probably desirous of complying with the request of their mentors to help in an accurate assessment of the program as a whole, rather than have individual alumni evaluated.

Given the apparent success of treatment in this cohort, however, we may consider what aspects of the program may have led to a positive outcome in this highly committed group. Rather than offering a cross-sectional representation of patients treated in the program, this cohort offers a perspective on the psychology of commitment to a program invested in the AA ethos. To this end, the singular role played by AA, rated by respondents as central to their rehabilitation, must be examined in relation to the allied medically operated modalities. As evident in each subject's responses, commitment was high to the AA ideology. Such commitment served as a basis for compliance with the physician-operated modalities in which AA involvement was couched. It also allowed patients to identify with program staff, who themselves subscribe to AA principles. Three psychological factors can be seen as influential to this process. They can be inferred from the observations made in this study on the respondents' attitude toward AA.

*Shared belief.* As evident in responses to scale items, subjects espoused an intense belief in AA, and the intensity of their commitment was highly correlated with their perception of why they were successful in maintaining a stable recovery. AA was understood to be more influential by respondents than the doctors who were responsible for their care. Most of the treating staff in the program had themselves had experience with 12-step programs, and this would probably lead to a strong reenforcement of beliefs throughout the treatment system. This parallels the bonding role of AA sponsorship in free-standing chapters (9) but stands in contrast to institutional treatments reported for impaired physicians, where AA is often not mentioned (10, 11) or only recommended after discharge (11, 12).

*Group cohesiveness.* The close camaraderie promoted by AA (13) stands in contrast to the clinical and more detached ambience of most psychiatric facilities. In the Impaired Physicians Program the strength of affiliative feelings was evident in the intense cohesiveness expressed toward fellow 12-step members. Subjects' responses indicated that they felt closer to their confreres in AA than they felt toward the outsiders they knew best; the magnitude of this cohesiveness was no different from that observed among members of a zealous, communal religious sect (2). The importance of this intensity of affiliation is underlined by the findings of Trice and Roman (14), who reported that affiliativeness was a principal predictor of engagement in AA. In addition, we have found in other zealous groups that such cohesive feelings are important reinforcers of compliance with group behavioral norms (6). They promote an alternative dependency; Vaillant and Milofsky have found this central to recovery from addiction (15).

*Mutual identification.* Acquiring a social role compatible with recovery accords the physician in the program a more stable abstinence, and this emerges as he or she assumes the role of a professional care giver in the addiction field. In the AA sponsorship process, the halfway houses, and the Caduceus peer-led groups, the physician is in close continuing contact with other physicians who have achieved a stable recovery. Twelve-step work or helping other addicts to abstain is a central AA theme, and all patients in the program spend an extended period of their halfway house time counseling substance abusers in community settings. Most ultimately become engaged in working in the addiction field to some extent. For example, almost half of the cohort, the more senior ones, were serving as AA sponsors. In this regard, they were monitors in a system that first transmits a regimen of abstinence to new members and later on inculcates the AA value system in them (16). Furthermore, an appreciable portion of respondents adopted addiction as their principal medical specialty after achieving recovery.

These observations can be considered in light of a perspective on AA as an ideologically oriented healing group. AA had its origins in the intense religious experience of Bill W (17), and its influence can be viewed as emerging from this leader, whose charismatic role is transmitted to successive generations of members (6). The group's values are thereby transmitted by means of their integration into the group's rituals and organizational structure. As evidenced here, this has been accomplished effectively in the case of the Impaired Physicians Program.

These observations reflect on the existing literature on treatment effectiveness in those settings where AA is combined with psychiatric care. Emrick (1) reviewed studies where both approaches were offered and found that the effect of AA on outcome was beneficial in most cases. The degree to which the AA model was integrated into the ethos of the treatment program in these settings, however, was highly variable. Our findings suggest that the effectiveness of a self-help program like AA, when offered to hospitalized patients, depends on how well its ethos is integrated into the psychotherapeutic treatment program. Effectiveness may also depend on how well the self-help program is built into an extended, structured aftercare program. More research should be done into ways of achieving such effective integration of self-help and psychiatric care, in order to achieve enhanced treatment outcome.

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# Hypnotizability of Psychiatric Inpatients According to Two Different Scales

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*Data on the hypnotizability of 113 psychiatric inpatients and 58 normal control subjects were compared. The patients' mean score on the Hypnotic Induction Profile was significantly lower than that of the control subjects, but on the Stanford Hypnotic Susceptibility Scale: Form C, these patients and control subjects did not differ significantly. On both scales rank-ordered scores of different diagnostic groups of the patients supported the theory that hypnotizability varies according to type of psychopathology. Some results, such as the hypnotizability of the schizophrenic patients, depended on which scale was used. This finding may explain the conflicting literature on the hypnotic potential of schizophrenic patients.*

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The purpose of this study was to assess whether a systematic relationship exists between specific types of psychopathology and hypnotic capacity, or hypnotizability. The study addressed 1) whether different diagnostic groups of psychiatric patients score in a predictable sequence relative to one another on standardized hypnosis scales and 2) whether the type of standardized hypnosis scale used can influence empirical results regarding the hypnotic capacity of psychiatric patients. Specifically, have conflicting results on previous tests of the hypnotizability of schizophrenic patients been due to the type of assessment instrument?

Hypnotizability is the inherent capacity of an individual to experience hypnosis. Individuals who are hypnotically responsive commonly report deep relaxation and/or bodily sensations of lightness. Those who are highly hypnotizable appear to have additional capabilities that allow them to temporarily experience "alterations in perception, memory, or mood" (1, p. 22). Highly hypnotizable individuals also display particular aptitudes and behaviors, such as an ability to become absorbed in vivid imagery and fantasy (2), when they are not in a hypnotized state. Approximately 10%–15% of the normal population is highly hypnotizable (3).

Whether hypnosis can be used safely and effectively with severely ill psychiatric patients has been widely debated for over 100 years; the majority of the literature has focused exclusively on psychotic or schizophrenic patients (4–9). In 1884 the French psychiatrist Voisin (10) observed that only 10% of psychotic patients were hypnotizable, and his contemporaries reported that hypnosis was "inefficient" for psychotic patients (5). Some 50 years later, Copeland and Kitching (11) stated that "cases which presented as true psychoses could not be hypnotized" (p. 328). However, over the last 40 years, there have been conflicting clinical reports regarding the hypnotizability of psychotic patients, including statements that psychotic patients cannot be hypnotized (12–14) and, alternatively, detailed reports of cases in which hypnosis was successfully used in the treatment of schizophrenic patients (6, 8, 15).

Empirical studies of the hypnotizability of schizophrenic patients have also yielded contradictory results. Investigators have reported that schizophrenic patients' hypnotic capacity is lower than (4, 5, 16, 17), the same as, or higher than (18–20) college student norms. Therefore, no clear-cut statements can be made regarding the hypnotizability of these patients.

Previous studies have primarily compared schizophrenic patients to normal subjects, thereby failing to allow for comparisons between schizophrenic and other patient groups where a broader perspective of hypnotizability and psychopathology could be addressed. In fact, rarely has a study investigated hypnotizability in multiple diagnostic groups. The one exception is the empirical work of Spiegel et al. (17), who made comparisons of measured hypnotizability among patients in four diagnostic groups. They found that all

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four groups (thought disorder, anxiety disorder, affective illness, and miscellaneous disorders) had significantly lower hypnotizability scores than control subjects (community volunteers). They concluded that "greater hypnotizability is associated with relative mental health" (p. 435). However, this conclusion needs to be understood in the context of studies which have reported that patients with specific psychiatric disorders are more hypnotizable than normal control subjects; that is, significantly higher hypnotizability has been reported in patients with phobia (21–24), bulimia (25), multiple personality disorder (26), and posttraumatic stress disorder (27).

Empirical findings regarding high hypnotic capacity in specific groups of patients have led some investigators to suggest a potential relationship between certain cognitive processes and specific types of symptom expression. For example, Frankel and Orne (21) proposed that the cognitive processes tapped during a hypnotic trance may also be involved in the development and maintenance of phobic symptoms. Pettinati et al. (25) found high hypnotizability in patients with bulimia and proposed that, as part of their disorder, these patients may spontaneously experience brief dissociative states during severe episodes of binge eating and purging.

Spiegel and Spiegel (16) have described what appears to be the only theoretical model of hypnotizability and psychopathology that attempts to include a spectrum of psychopathology. They have proposed that a psychiatric patient's hypnotic capacity will predict his or her specific psychopathological profile; the rationale is that certain personality traits underlie particular clusters of disorders.

In Spiegel and Spiegel's proposed model of hypnotizability and psychopathology, the relationship is viewed on a continuum. The least hypnotizable patients include those with "schizophrenia, obsessive-competitive (compulsive) disorder, and/or paranoia." Patients with medium to high hypnotic capacity include those with an "affective disorder, impulse disorder, or passive-aggressive disorder." High hypnotizability signals "hysterical disorders" (16, p. 133).

Unfortunately, lack of empirical work and development of alternative models have prevented evaluation of the usefulness of Spiegel and Spiegel's model. Of the work that has been done, the most relevant to their model is the finding of low hypnotizability in schizophrenic patients (17). As noted, however, this finding has not been consistently reported, although the present study focused on a possible confounding variable in previous research: the type of hypnosis scale used. Frischholz (28) and his colleagues, using a meta-analysis, retrospectively reviewed 28 studies that compared the hypnotizability of schizophrenic subjects to that of a normal control group. They reported that 56% of the variance was accounted for by the hypnosis scale administered. This retrospective finding requires replication by a prospective look at two different hypnosis scales administered to the same patients. It may simply be that the inconsistent results of different studies have been produced by using different hypnosis scales.

By comparing the levels of hypnotizability of patients in five diagnostic groups, we hoped to empirically examine the relationship of hypnotizability to psychopathology. By using two standardized hypnosis scales, the Hypnotic Induction Profile (16) and the Stanford Hypnotic Susceptibility Scale: Form C (29), with the same subjects, we hoped to clarify why some studies have reported lower levels of hypnotizability in schizophrenic subjects while other studies have not.

We also proposed to compare our results with the predictions generated by the model of Spiegel and Spiegel. In the present study, our interest in this model was not to investigate hypnotizability as a diagnostic tool (as Spiegel and Spiegel have emphasized), but rather to determine whether the level of hypnotic capacity in psychiatric patients is associated with specific diagnostic profiles. That is, would patients in some specific diagnostic groups be more hypnotizable than others? While the diagnostic terminology in the Spiegel and Spiegel model is dated, we felt that it should be possible to determine approximately where on the continuum certain groups of patients with *DSM-III* diagnoses would fall with respect to hypnotizability.

## METHOD

### *Subjects*

This investigation included 171 volunteer subjects: 113 psychiatric patients and 58 normal control subjects. The subjects were primarily Caucasian and from middle- to upper-income families. Thirty-six percent (N=62) of the subjects were male. While the majority of patients who were approached agreed to participate in the study, there were a number of patients who met the inclusion criteria but whose attending psychiatrists did not want them to participate because they were actively psychotic, extremely anxious, or predictably uncooperative. Although the number of physician refusals was not recorded, it is fair to say that only cooperative and highly motivated patients whose symptoms were relatively controlled at the time of the hypnotic evaluation participated in the study.

The patient groups consisted of 113 psychiatric inpatients at the Carrier Foundation, an acute care, private, nonprofit psychiatric hospital. The mean age of the patients was 28.6 years (range=14–78 years). The diagnostic groups we selected represented the most frequent diagnoses, acording to *DSM-III* criteria, of the patients admitted for inpatient treatment at the Carrier Foundation: 1) schizophrenic disorders (N=28; 32% female; 79% paranoid type, i.e., having persecutory or grandiose delusions or hallucinations with persecutory or grandiose content), 2) major depression (N=20; 90% female; 100% unipolar, without melancholia and/or psychotic features), 3) substance use disorders (N=23; 35% female; 26% having alcohol dependence with no other drug dependence, 30% drug dependence without alcohol dependence, and 44% both alcohol and drug dependence), 4) anorexia nervosa (N=19; 100% female; 100% restricting type, i.e., using starvation rather than purging to lose weight), and 5) bulimia (N=23; 95% female). The anorexia nervosa and bulimia groups constituted part of the patient group described and reported earlier by Pettinati et al. (25).

The hospital has specialized intensive treatment programs (individual, family, behavioral, and pharmacological) for the full range of psychiatric disorders in adults and adolescents. The average length of inpatient stay is just over 30 days. During the 2- to 3-week study period, 100% of the 28 patients with schizophrenic disorders were taking antipsychotic medication, and 100% of the 20 patients with major depression were taking antidepressant medication. The majority of the patients with substance use disorders or eating disorders (anorexia nervosa or bulimia) were not taking prescribed psychotropic medications during the study period. Through medical chart review it was determined that all of the patients in the study showed some improvement over the course of inpatient treatment.

Published data on 58 Stanford University students reported in a study by Orne et al. (30) served as the normal control data. This group of students was chosen because each had been administered both the Hypnotic Induction Profile and the Stanford Hypnotic Susceptibility Scale: Form C.

### *Instruments*

The Hypnotic Induction Profile is a 10-minute, 10-point scale that is administered individually to the patient, usually by the treating clinician, who has received training in using the instrument. A rapid hypnotic induction that includes instructions to look upward and then roll the eyes is followed by a suggestion to raise an arm and then by a procedure for leaving the trance. The clinician elicits patient self-reports of the experience during and following the trance, for example, "Does your left hand feel as if it is not as much a part of your body as your right hand?" (16, p. 48). The authors of the Hypnotic Induction Profile have reported that the test-retest and interrater reliabilities for two patient groups (16, 31) were 0.75 and 0.76, respectively.

The Stanford Hypnotic Susceptibility Scale: Form C is an individually administered 50-minute, 12-item scale that includes a hypnotic induction (suggestions for eye fixation, eye closure, and relaxation) followed by a series of 12 discrete motor and cognitive suggestions, for example, "I want you to think of something sweet in your mouth . . . like a little sugar . . . the sweet taste is increasing . . . sweeter and sweeter" (29, p. 19). The Stanford scale, form C, was selected primarily because it has been used in studies that have measured the hypnotizability of schizophrenic patients and "is generally regarded as the best available criterion of hypnotizability" (32, p. 93). In the test manual (29), the authors of the Stanford scale reported a reliability coefficient (Kuder-Richardson) of 0.85 for a college student sample.

On both of the instruments the content is unrelated to clinical treatment, and a higher score indicates greater hypnotic capacity. Hypnotic Induction Profile scores can range from 0 to 10. According to Spiegel and Spiegel (16, p. 157), a score of 0 to 6 indicates low hypnotic capacity, 6.25 to 9 indicates medium capacity, and 9.25 to 10 indicates high capacity. For the Stanford scale, form C, scores can range from 0 to 12, and there are standard ranges for defining low (0–4), medium (5–7), and high (8–12) hypnotizability (29, p. 45).

### *Procedure*

Patients meeting the *DSM-III* criteria for any of the five diagnostic groups were asked to volunteer for a hypnotic assessment. Each diagnosis was made by the attending psychiatrist and reviewed by a research staff member who had personally interviewed the patient over time and had reviewed the patient's chart. If there was any question about the diagnosis, the psychiatrist investigator for this study (R.L.H.) reviewed the case in question.

The patients were told that the assessment was independent of their treatment and that hypnosis might or might not be used in their therapeutic treatment plans. Regardless of which hypnosis scale was used, all hypnotic sessions were preceded by a discussion to establish rapport and were followed by a discussion of the patient's experiences during the session. The hypnotist's blindness to patient diagnosis was maintained as much as possible; sometimes it was broken during the hypnosis session because the patient displayed characteristic symptoms unique to his or her disorder.

The Hypnotic Induction Profile was given within 2 weeks following admission, and the Stanford scale, form C, was scheduled approximately 2 weeks after that. Counterbalancing the order of administering the two scales was not appropriate because the Stanford scale was not designed to be a first exposure to hypnosis (29). Therefore, the Harvard Group Scale of Hypnotic Susceptibility: Form A (33) was used for counterbalancing and was administered within 48 hours of the Hypnotic Induction Profile. Approximately half the patients were given the Harvard scale first and half were given the Hypnotic Induction Profile first, so that the latter would not always be the first hypnotizability scale in the procedure. The Harvard scale, form A, has been reported to correlate significantly (r=0.59, p<0.001) with the Stanford scale, form C (34), and can be given as the first exposure to hypnosis (33). In addition, monitoring the results of the Harvard scale would allow us to determine which changes in hypnotizability scores were due to an improved clinical state and better motivation between the

**TABLE 1. Scores on Two Hypnotizability Scales for Patients in Five *DSM-III* Diagnostic Categories and for Normal Control Subjects**

| | Patient Group | | | | | | Analysis | | |
|---|---|---|---|---|---|---|---|---|---|
| Item | Anorexia Nervosa (N=19) | Schizophrenic Disorders (N=28) | Major Depression (N=20) | Substance Use Disorders (N=23) | Bulimia (N=23) | Normal College Students (N=58) | F | df | p |
| Age (years) | | | | | | | | | |
| Mean | 18.4 | 29.3 | 38.6 | 33.9 | 22.3 | 22.9 | 13.1 | 5, 165 | <0.001 |
| SD | 3.6 | 13.1 | 17.6 | 14.5 | 6.5 | 4.0 | | | |
| Hypnotic Induction Profile score | | | | | | | | | |
| Observed mean | 4.66 | 4.90 | 5.49 | 7.27 | 6.97 | 6.73 | 5.0 | 5, 165 | <0.001 |
| SD | 3.1 | 2.9 | 2.9 | 1.8 | 2.5 | 2.2 | | | |
| Adjusted mean[a] | $4.23_a$ | $4.98_{a,b}$ | $6.00_{b,c,d}$ | $7.57_e$ | $6.72_{c,d,e}$ | $6.51_{d,e}$ | 5.5 | 5, 164 | <0.001 |
| Stanford scale[b] score | | | | | | | | | |
| Observed mean | 5.00 | 5.82 | 7.20 | 7.26 | 7.52 | 6.12 | 3.4 | 5, 165 | <0.01 |
| SD | 2.3 | 1.8 | 2.3 | 2.5 | 1.8 | 3.1 | | | |
| Adjusted mean[a] | $4.92_f$ | $5.83_{f,g}$ | $7.28_{g,h}$ | $7.31_{h,i}$ | $7.48_h$ | $6.08_{f,g,i}$ | 3.3 | 5, 164 | <0.01 |

[a] Adjusted means were corrected for age by multivariate analysis of covariance. Adjusted means with the same subscript are not statistically different at $p<0.05$ according to Duncan's multiple range test.
[b] Stanford Hypnotic Susceptibility Scale: Form C.

times the Hypnotic Induction Profile and the Stanford scale, form C, were administered (2–3 weeks). Studying the results of the Harvard scale, form A, would allow us to see whether this scale yielded findings more similar to those of the Hypnotic Induction Profile or to those of the Stanford scale. All of the results of the Harvard scale are not reported in this paper because of space limitations; however, the results that relate specifically to concerns about potential changes in hypnotizability due to therapeutic improvement and/or changes in motivation are presented.

## RESULTS

### *Hypnotizability Scores*

*Hypnotic Induction Profile.* The mean±SD Hypnotic Induction Profile score of the inpatients (5.87±2.8) was significantly lower than that of the normal college students (6.73±2.2) ($t=-2.21$, $df=169$, $p<0.05$, two-tailed test). This replicates the results of Spiegel et al. (17), who reported that psychiatric patients, regardless of diagnosis, had significantly lower Hypnotic Induction Profile scores than normal control subjects.

*Stanford Hypnotic Susceptibility Scale: Form C.* The inpatients' mean±SD Stanford scale score (6.57±2.3) was not significantly different from that of the normal students (6.12±3.1) ($t=0.96$, $df=169$, n.s.) and was in the direction opposite to the results with the Hypnotic Induction Profile. This finding suggests that the average hypnotizability scores of psychiatric patients are *not* different from those of normal control subjects.

*Harvard Group Scale of Hypnotic Susceptibility: Form A.* The inpatients' mean Harvard scale score (7.53±2.6) was not significantly different from that of the normal students (6.98±2.7) ($t=1.29$, $df=169$, n.s.) and, as with the Stanford scale, was in the direction opposite to the results with the Hypnotic Induction Profile. This finding for the Harvard scale also suggests that the average hypnotizability scores of psychiatric patients are *not* different from those of normal control subjects. For the patient groups, the order in which the Hypnotic Induction Profile and the Harvard scale were administered did not affect the response on the Harvard scale: the mean±SD score on the Harvard scale was 7.3±2.6 when that scale was given first and 7.6 ±2.6 when it was given second ($t=0.73$, $df=104$, n.s.) (order information was missing for seven patients).

In summary, when the same patients were administered different hypnosis scales, the conclusions to be drawn concerning hypnotizability of psychiatric patients were inconsistent across the scales. The evaluation of a patient's hypnotic capacity depended on the standardized hypnotizability scale used.

### *Hypnotic Induction Profile Versus Stanford Scale in Patient Groups*

The mean ages for each of the five diagnostic groups and the normal control group are presented in table 1. A one-way analysis of variance found significant differences among the groups with respect to age. Since age has been previously shown to correlate negatively with hypnotizability (16, 35), all analyses were done with age as the covariate. Age was a significant covariate for the Hypnotic Induction Profile ($F=4.8$, $df=1, 164$, $p<0.03$) but not for the Stanford scale ($F=0.69$, $df=1, 164$, n.s.).

The mean hypnotizability scores (both observed and adjusted for age) for the Hypnotic Induction Profile and for the Stanford scale can be seen in table 1. We conducted a multivariate analysis of covariance, with age as the covariate, that included simultaneously the six groups' mean scores on the Hypnotic Induction Profile and on the Stanford scale. The results were highly significant (F=4.36, df=10, 328, p=0.001). All comparisons between individual groups were made using Duncan's multiple range test (36). These comparisons were made for the observed and the adjusted means. The significant differences between any two groups are indicated in table 1 by subscripts. Although for clarity subscripts are presented for the adjusted means only, the results did not substantially differ when comparisons were made using the observed means, with two exceptions. On the Hypnotic Induction Profile the observed mean for the anorexia nervosa group did not statistically differ from that for the major depression group, and on the Stanford scale the observed mean for the schizophrenic disorders group did not statistically differ from that for the substance use disorders group.

The main effects from the multivariate analysis of covariance for both scales were significant: for the Hypnotic Induction Profile, F(observed)=5.0, F(adjusted)=5.5, df=5, 164, $p<0.0001$; for the Stanford scale, F(observed)=3.4, F(adjusted)=3.3, df=5, 164, $p<0.007$. These findings indicate that among groups, levels of hypnotizability according to the Hypnotic Induction Profile and the Stanford scale, form C, were significantly different.

### *Patient Groups Versus Normal Control Subjects*

On the Hypnotic Induction Profile, Duncan's multiple range test revealed that patients with anorexia nervosa, restricting type, or schizophrenic disorders scored significantly lower than normal control subjects. The patients with major depression, substance use disorders, or bulimia did not differ statistically from the normal control subjects.

On the Stanford scale, Duncan's multiple range test revealed that the mean scores were not statistically different between any of the patient groups and the normal control subjects except for the bulimic patients, who had a significantly higher mean score than the control subjects.

On the Harvard scale, the mean score of the normal control subjects did not differ statistically from that of any of the diagnostic groups of patients. Particularly interesting is the comparison of the schizophrenic patients and the normal control subjects: mean±SD scores=7.14±2.3 and 6.98±2.7, respectively. This difference was not statistically significant and was in the direction opposite to the finding for the schizophrenic patients compared to the normal control subjects on the Hypnotic Induction Profile. Thus, the interpretation of how patients' hypnotizability compared to that of normal subjects differed, depending on which patient group was studied and which hypnotizability scale was used.

### *Hypnotizability Among Patient Groups*

In addition to comparisons with normal control subjects, all patient groups were compared with each other by using the Duncan multiple range test. Again, for the most part, in comparisons of two patient groups, the interpretation of differences in hypnotizability depended on which standardized scale was used. For example, according to the Hypnotic Induction Profile, patients with substance use disorders had a significantly higher mean hypnotizability score than patients with major depression, but on the Stanford scale the groups scored similarly.

Despite these divergent results, one similarity between the results of the two scales emerged: the rank order of the group mean hypnotizability scores of the 113 patients in the five diagnostic groups was similar (Pearson's r=0.51, df=112, $p<0.01$, two-tailed). The rank order of the mean Stanford scale scores (for patient groups only) served as the basis for structuring table 1 from left to right. On both the Hypnotic Induction Profile and the Stanford scale, the lowest levels of hypnotizability were in the restricting anorexia nervosa group and in the schizophrenic disorders group. Patients with bulimia or substance use disorders had the highest group mean hypnotizability scores

It is interesting that the rank ordering of the hypnotizability scores seen in table 1 roughly approximates what might be predicted using Spiegel and Spiegel's model if the five diagnostic groups were ranked on a continuum from primarily cognitive to primarily affective psychopathology. The extreme differences in scores between the anorexic patients and the bulimic patients, which may seem inconsistent, might be understood by also comparing the two groups on MMPI measures of hysteria, a dimension purported by the model to be associated with high hypnotizability. None of the 19 anorexic patients scored in the deviant range (i.e., T score greater than 70) on the MMPI hysteria scale, whereas 65% (N=15) of the 23 bulimic patients did so. Also, anorexic patients' low hypnotizability scores may reflect their typically obsessive and/or compulsive personality features (37), a dimension purported by the model to be associated with low hypnotizability.

## DISCUSSION

The Hypnotic Induction Profile may be a difficult scale for certain types of patients and easier, by comparison, for normal subjects. For example, to score high on that scale, one must achieve some degree of dissociation, have insight into bodily sensations, and be able to verbalize subjective experiences, all in a very brief period of time. Most schizophrenic patients will have difficulty with these tasks. It is not clear whether this difficulty results from an underlying dysfunction in cognitive processing that has been hypothesized to occur in individuals with thought disorder (38). Lavoie and Elie (39) have proposed that illogical thought patterns in certain stages of psychotic illness may reflect a failure in information processing that will not allow an individual to experience hypnosis. Alternatively, Brown (40) has suggested that a primary deficit in schizophrenic disturbance is lack of awareness of internal sensations and feelings. These need to be experienced in order for a person to respond to questions on the Hypnotic Induction Profile. Finally, schizophrenic patients may become anxious when asked to focus on bodily sensations and therefore may be unable to respond to the questions on the Hypnotic Induction Profile. Even if schizophrenic patients can experience hypnotic dissociation and have insight into their subjective experiences, they may score low on this scale because they have difficulty articulating these kinds of experiences.

It should be noted, however, that all of these tasks might be easier for schizophrenic patients if they could be performed at a slower pace. Schizophrenic patients' slower speed of information processing (38) may require a slower hypnotic induction period. In fact, the reason schizophrenic patients performed better on the Stanford scale, form C, may be that the longer hypnotic session allowed patients with severe cognitive disorders to make a more gradual transition into a dissociated state.

While it is possible to have inappropriately high scores on the Stanford scale, form C, due to behavioral compliance, good discussion sessions both before and after the hypnosis sessions usually lessen the possibility of invalid hypnosis scores. However, on a few of the Stanford scale suggestions, such as the one for amnesia, it is possible to have a "passing" score by *not* responding. The schizophrenic patients in this study "passed" the suggestion for amnesia significantly more frequently than the normal subjects (57% and 36%, respectively; p=0.05, Fisher's exact probability test). This finding has also been reported independently (41, 42).

Another issue is whether schizophrenic patients' more frequent responses to suggestions that require vivid imagining reflect spontaneous hallucination and therefore do not provide an index of a hypnotic state. There was a trend in this study for the schizophrenic patients to respond more frequently than the normal control subjects to the suggestion on the Stanford scale to "see and hear a mosquito" (82% and 67%, respectively; p=0.11, Fisher's exact probability test).

Finally, in this study the standard deviation of the Stanford scale score for the schizophrenic group was significantly smaller than the standard deviation for the normal control subjects (Bartlett-Box test for homogeneity of variance, F=9.3, df=1, 84, p=0.002). Approximately 60% of the 28 schizophrenic patients scored in the medium hypnotizability range on the Stanford scale, compared to 29% of the 58 students ($\chi^2$=7.8, df=2, p=0.02). This finding is consistent with Lavoie and Elie's observation (39) that several studies have reported a smaller dispersion of schizophrenic patients' hypnotizability scores clustering around the mean in the medium range of hypnotizability. This suggests that while the mean scores of the schizophrenic patients and normal subjects may appear similar, the nature of the hypnotic response may be different. Overall, differences between the Hypnotic Induction Profile and the Stanford scale, form C, need to be explored across a variety of patient groups in future studies.

While the two hypnotizability scales used in this study clearly have some different properties, it is of interest that the rank order of group mean hypnotizability scores was similar for the Hypnotic Induction Profile and the Stanford scale, form C. That is, anorexic and schizophrenic patients scored lower in hypnotizability than those with major depression, substance use disorders, or bulimia. This rank ordering appears to roughly approximate Spiegel and Spiegel's model, where schizophrenic patients rank lower on hypnotizability than those with affective, impulsive, and/or hysterical symptoms. However, it would be premature to draw any firm conclusions until more refinement and updating of the model takes place. Our reason for referring to this model is to stimulate the development of theoretical models in this important area of scientific inquiry.

In conclusion, there is a need for more studies of hypnotizability in a variety of different clinical populations. Attending to the nature of the hypnotizability scale will, we hope, generate further work on the nature of the differences in hypnotizability scales, particularly with respect to deciding whether one scale is preferable for certain kinds of patients. Also, the development of a comprehensive model of hypnotizability and psychopathology would have important implications for understanding the cognitive mechanisms that mediate hypnotizability as well as different types of psychopathology. Resolving these issues could possibly provide useful information for clinicians in deciding which patients might benefit most from hypnotic techniques in therapy. Using hypnotherapeutic techniques as an adjunct to the treatment regimens of patients who are highly hypnotizable may significantly improve their treatment outcome.

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# The Structured Clinical Interview for *DSM-III-R* Dissociative Disorders: Preliminary Report on a New Diagnostic Instrument

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*The authors describe the Structured Clinical Interview for DSM-III-R Dissociative Disorders (SCID-D), which investigates five groups of dissociative symptoms (amnesia, depersonalization, derealization, identity confusion, and identity alteration) and systematically rates both the severity of individual symptoms and the evaluation of overall diagnosis of dissociative disorder. Preliminary findings from a study of 48 subjects with and without psychiatric diagnoses indicate good to excellent reliability and discriminant validity for the SCID-D as a diagnostic instrument for the five dissociative disorders and as a tool for the evaluation of dissociative symptoms encountered within nondissociative syndromes.*

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Until now there has been no standardized instrument designed to yield uniform clinicians' diagnoses of the dissociative disorders. *DSM-III-R* defines the essential feature of the dissociative disorders as "a disturbance or alteration in the normally integrative functions of identity, memory, or consciousness." The fact that dissociative disorders may mimic a spectrum of psychiatric conditions—including the psychotic, affective, and character disorders—complicates accurate assessment. Specifically, patients with a dissociative disorder may experience hallucinations and/or first-rank symptoms, which may contribute to diagnostic confusion with schizophrenia (*DSM-III-R*; 1–4); depressive symptoms, which contribute to confusion with affective disorders (1–4); and a chaotic life style, which contributes to confusion with borderline personality disorder (*DSM-III-R*; 1–5). Several studies have indicated that the dissociative disorders may be underdiagnosed and that identification as well as appropriate treatment of patients with these disorders may be delayed (1–4, 6). Uniform diagnoses of other psychiatric disorders have been furthered by the use of standard criteria and structured clinical interviews (7–10). However, diagnostic instruments developed for other psychiatric categories are not oriented toward the specific patterns of underlying dissociative pathology. Neither the Schedule for Affective Disorders and Schizophrenia (SADS) (9) nor the Diagnostic Interview Schedule (DIS) (10), two of the most commonly used standardized tools, includes scales for the dissociative disorders, and no data are currently available on the scores obtained by patients with dissociative disorders on these standard measures.

Current instruments specific to the dissociative disorders were designed as screening devices or symptom rating scales rather than as primary diagnostic instruments and are not meant to yield clinical diagnoses of dissociative disorders. Among these instruments are the Dissociative Experiences Scale (11) and the Questionnaire of Experiences of Dissociation (12), two self-report screening instruments that rate dissociative experiences and for which reliability and validity have been reported. Another screening instrument is the Perceptual Alteration Scale (13), which is in preliminary stages of development. Other self-report questionnaires focus on the symptom of depersonalization (14–16). Self-report formats may be problematic for diagnosis of the dissociative disorders, since patients with dissociative disorders are often reluctant to describe or may be entirely unaware of symptoms such as amnesia or identity alteration and therefore unable to complete an accurate self-report.

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The Structured Clinical Interview for DSM-III-R Dissociative Disorders (SCID-D) was developed to yield *DSM-III-R* diagnoses of dissociative disorders. It uses a structured interview format modeled on the Structured Clinical Interview for DSM-III-R (17). In this report we describe the characteristics of the SCID-D and present preliminary findings on its reliability and discriminant validity.

## THE INSTRUMENT

The SCID-D contains 200 items, including follow-up questions, that are designed to evaluate five symptom areas (amnesia, depersonalization, derealization, identity confusion, and identity alteration) as well as the *DSM-III-R* criteria for dissociative disorders. Amnesia represents a specific and substantial block of time that cannot be accounted for by memory. Depersonalization refers to detachment from oneself—a sense of "going through the motions" or of looking at oneself as an outsider. Derealization refers to the sense that one's surroundings are unreal. For the purposes of the SCID-D, the symptom areas of identity confusion and identity alteration were developed and are now an integral part of the SCID-D. Identity confusion refers to subjective feelings of confusion, uncertainty, or puzzlement centered on patients' knowledge of their own identity. Identity alteration focuses on behavioral manifestations of identity confusion, such as exhibiting a special knowledge or skill without knowing how this skill was acquired.

Items within each symptom area proceed from general, open-ended screening questions to detailed follow-up questions that systematically explore the characteristic features of the symptom. Each positive response is followed by questions such as, "What was that experience like? How often has this happened?" in order to determine the nature and frequency of the episode. This sequence elicits spontaneous, subjective descriptions of endorsed features before specific follow-up questions are asked. To date, subjects have found the interview to be nonthreatening and easily understandable. The time required to administer the interview ranges between 10 and 20 minutes for normal subjects, 20 and 50 minutes for patients with nondissociative psychiatric disorders, and 40 and 70 minutes for patients with dissociative disorders.

The SCID-D modifies some features of the structured interview format to incorporate interview strategies specific to the dissociative disorders. Due to the complex nature of dissociative symptoms, several questions may be asked about a single symptom in order to investigate different facets or descriptive styles for that symptom. For example, subjects may variously describe depersonalization as watching the self from outside of the body, being a stranger to oneself, or feeling like an automaton. The same subject may endorse feeling like an automaton but deny watching the self from outside of the body. Either description represents a manifestation of the single symptom of depersonalization as defined by *DSM-III-R* (criterion A for depersonalization disorder). Inconsistent responses to several interview items regarding a single symptom do not invalidate results because, in fact, such differences may be a manifestation of the symptom under investigation. In addition, the SCID-D interviewer notes nonverbal behavioral cues that are characteristic of the dissociative disorders, such as amnesia for events that occurred during the interview. Examples of the interview questions for the symptom of depersonalization are given in appendix 1.

The SCID-D scoring manual provides diagnostic score sheets for each of the disorders. These contain specific SCID-D criteria developed to operationalize the more general *DSM-III-R* criteria (see appendix 2). There is no one-to-one correspondence between single interview items and diagnostic criteria, and scoring relies on the combination of specific interview items. The appropriate combination of items to meet *DSM-III-R* criteria is specified on the diagnostic score sheets. For ease of scoring, all diagnostic criteria are cross-referenced with all appropriate interview items. Rating sheets also include a final check for the presence of any features that exclude a dissociative diagnosis (e.g., the dissociative symptoms occurred only when the subject ingested drugs or alcohol).

The interview is designed to be administered by an experienced clinician trained in its proper administration and evaluation. Training enables the clinician to use operationally defined clinical criteria to make global severity ratings of the five symptom areas based on anchored judgments. The SCID-D scoring manual contains severity ratings for each of the five dissociative symptoms in terms of the frequency and duration of episodes and the presence or absence of precipitating stressors. The SCID-D involves the clinician's judgment of 1) whether a given symptom is present, 2) whether the *DSM-III-R* criteria for a dissociative disorder have been met, and 3) whether a past dissociative episode has occurred from which there has been recovery. A clinician trained in administration and evaluation of the SCID-D rates the patient's responses during the interview and summarizes the results using the SCID-D diagnostic score sheets. Score sheets require 5 to 10 minutes after the interview to complete.

## METHOD

One of us (M.S.) administered 48 consecutive SCID-Ds and scored the subjects' responses to individual items as the interview proceeded. Following the interview, she completed SCID-D diagnostic score sheets and a global rating scale of the individual dissociative symptoms. Because the patients came from a clinical setting familiar to the interviewer, she was not blind to the referring clinicians' diagnoses of 15 of the patients. The video- or audiotaped interviews were scored independently by a co-rater, a psychiatric nurse who was

**TABLE 1. Agreement of Two Raters Using the Structured Clinical Interview for DSM-III Dissociative Disorders (SCID-D) to Assess Psychiatric Patients and Normal Control Subjects**

| Level of Analysis | N | Overall Diagnostic Agreement (%) | Level of Chance-Corrected Agreement[a] |
|---|---|---|---|
| Total SCID-D score | 48 | 92 | 0.95[b] |
| Presence or absence of a dissociative disorder | | | |
| Presence | 25 | 96 | 0.92[c] |
| Absence | 23 | 96 | 0.92[c] |
| Overall | 48 | 96 | 0.92[c] |
| Type of dissociative disorder | | | |
| Multiple personality | | 93 | 0.90[c] |
| Rater 1 | 8 | | |
| Rater 2 | 7 | | |
| Dissociative disorder not otherwise specified | | 93 | 0.82[c] |
| Rater 1 | 14 | | |
| Rater 2 | 16 | | |
| Depersonalization disorder | | 67 | 0.65[c] |
| Rater 1 | 2 | | |
| Rater 2 | 1 | | |
| Total | | 92 | 0.84[c] |
| Rater 1 | 24 | | |
| Rater 2 | 24 | | |
| Dissociative symptom | | | |
| Depersonalization | 48 | 95 | 0.88[d] |
| Derealization | 48 | 89 | 0.76[d] |
| Amnesia | 48 | 81 | 0.59[d] |
| Identity confusion | 48 | 90 | 0.78[d] |
| Identity alteration | 48 | 86 | 0.69[d] |

[a] All levels of chance-corrected agreement were highly statistically reliable ($p<0.05$ to $p<0.00001$). In terms of clinical significance, the guidelines of Cicchetti and Sparrow (21) and Fleiss (20) were used: below 0.40=poor, 0.40–0.59=fair, 0.60–0.74=good, and 0.75–1.00=excellent.

[b] The intraclass correlation coefficient ($R_I$, model II) (19, 22) was applied. This takes into account the fact that the same two examiners were used throughout. The level of observed agreement was obtained by using the formula $[(1-\Sigma \mid \text{DIFF} \mid)/(\Sigma \mid \text{DIFF} \mid_{\max}) \times 100]$, in which $\mid \text{DIFF} \mid$ refers to the absolute interexaminer difference in total SCID-D score for a given subject (e.g., $15-20=5$). See Cicchetti and Conn (23) and Robinson (24) for further details.

[c] Kappa (22) was applied because the data were nominally scaled.

[d] Weighted kappa (25) was applied because the data were ordinally scaled.

blind to all of the patients' referring clinicians' diagnoses. To minimize inadvertent cuing of the co-rater, M.S. did not skip a section if previous questions were answered in a clinically insignificant manner.

To allow us to administer the SCID-D to as wide a variety of subjects as was clinically feasible, the 48 subjects who participated in the study included 41 psychiatric patients with a range of axis I diagnoses as well as seven normal control subjects. The psychiatric subjects were outpatients in active treatment at the Connecticut Mental Health Center or in private therapy with Yale School of Medicine faculty. They had been in treatment with the referring physician for at least 6 months. Referring clinicians' diagnoses were based on *DSM-III-R* criteria and included schizophrenia (N=8), major depression (N=8), and other axis I disorders (posttraumatic stress disorder and generalized anxiety disorder) (N=7), along with dissociative disorders (N=18). One patient had depersonalization disorder, eight had multiple personality disorder, and nine had dissociative disorder not otherwise specified. Twelve of the patients had coexisting borderline or mixed personality disorders. The psychiatric patients were between 20 and 64 years old and had no evidence of organic brain syndrome or mental retardation. Any patients who were very agitated, gravely disabled, or at risk of suicide were excluded from participation in the study.

Most of the psychiatric patients and control subjects were women: 13 of the 18 patients with dissociative disorders, 16 of the 23 patients with nondissociative psychiatric disorders, and six of the seven normal control subjects. The subjects were also of similar ages: the mean±SD age of the patients with dissociative disorders was 34.8±6.9 (range=23–49 years), for the patients with nondissociative psychiatric disorders it was 40.6±9.6 years (range=26–62), and for the normal control subjects it was 34.3±13.5 years (range=20–64).

The clinical diagnoses of the 41 patients were made by the referring clinicians on the basis of a comprehensive assessment based on all available data, including psychological tests, past records, and observation over a 6-month period.

The normal control subjects were volunteers who responded to announcements at a local civic organization and at the Yale School of Medicine. Subjects from the community were excluded if they had a history of past outpatient treatment for a psychiatric disorder, psychiatric hospitalization, or suicide attempts.

The administration of the SCID-D was videotaped or audiotaped. Informed consent, including consent to video- and audiotaping, was obtained from all subjects.

## RESULTS

### *Reliability*

The diagnostic reliability of the SCID-D was examined at four levels of analysis: total SCID-D assessments, presence versus absence of a dissociative disorder, type of dissociative disorder, and specific dissociative symptoms.

Since the five SCID-D symptoms can each be scored on a 4-point scale (1=none, 2=mild, 3=moderate, and 4=severe), total SCID-D scores could range between a low of 5 (1×5) and a high of 20 (4×5). The intraclass R (19, 20) for interrater agreement on the total SCID-D score was 0.95 (see table 1).

For the determination of presence versus absence of a dissociative disorder, diagnostic information was categorized as indicating absence of dissociative disorder, presence of subthreshold disorder, or presence of dissociative disorder. The diagnosis of a dissociative disorder was assigned to 25 of the 48 subjects by each examiner. The diagnosis of a nondissociative psychiatric disorder was applied to 22 of the remaining 23 patients by M.S. and to 21 of the 23 patients by the second rater. Thus, the subthreshold diagnosis was applied to only one patient by M.S. and to two patients by the co-rater. Given the infrequency of use of the subthreshold diagnosis, this nosologic category was combined with the category of nondissociative psychiatric disorder, resulting in the same number of examiner diagnostic assignments (23 patients) to the nondissociative disorder category. There was 96% agreement between the two raters on both dissociative and nondissociative categories, with a kappa of 0.92 (see table 1).

The nominal diagnostic category of type of dissociative disorder comprised the five dissociative disorders in *DSM-III-R*: multiple personality disorder, psychogenic fugue, psychogenic amnesia, depersonalization disorder, and dissociative disorder not otherwise specified. Reliability assessment (22) indicated a high overall diagnostic agreement level as well as high levels of agreement between the raters for multiple personality and for dissociative disorder not otherwise specified (see table 1). Depersonalization disorder, a diagnosis applied to two patients by M.S. and to only one by the co-rater, produced a lower diagnostic agreement level and kappa (see table 1). These values were obviously restricted by the small number of patients on which they were based. Six patients presented symptoms of psychogenic amnesia or psychogenic fugue and also met criteria for multiple personality disorder or dissociative disorder not otherwise specified. *DSM-III-R* criteria specify that psychogenic amnesia and psychogenic fugue are to be diagnosed only in the absence of multiple personality disorder. Since symptoms of psychogenic amnesia and psychogenic fugue were subsumed by the diagnoses of multiple personality, only three diagnostic categories were used for purposes of analysis—depersonalization disorder, multiple personality, and dissociative disorder not otherwise specified.

For the analysis of specific dissociative symptoms, each symptom was scored on a dichotomous ordinal scale of measurement in which the symptom could be classified as absent, mild, moderate, or severe (21). Weighted kappa statistics (25, 26) were used for each symptom area separately. These ranged from 0.59 to 0.88; the corresponding levels of observed agreement were between 81% (amnesia) and 95% (depersonalization). A more detailed summary of these results is given in table 1.

In summary, the results of interexaminer reliability levels of individual SCID-D responses, whether based on total overall assessment, presence or absence of a dissociative disorder, type of dissociative disorder, or specific dissociative symptom, produced values that were almost uniformly in the good to excellent range of clinical significance (20, 21).

### *Discriminant Validity*

One objective of the study was to design a diagnostic instrument that would identify as positive all those patients previously diagnosed as having dissociative disorders by clinicians' diagnoses. In addition, the new instrument was expected to be capable of detecting one or more patients previously diagnosed by the referring clinician as not having a dissociative disorder. There was no a priori knowledge of whether the SCID-D would also miss patients previously diagnosed as having a dissociative disorder, and this possibility was also examined. Those positive SCID-D diagnoses which disagreed with clinicians' diagnoses were of special interest due to reports of underdiagnosis of these disorders (1–4, 6). Therefore, we investigated whether these positive SCID-D diagnoses were later confirmed by an independent source.

Data analyses were conducted of the extent to which SCID-D diagnoses significantly distinguished the 18 patients with referring clinicians' diagnoses of dissociative disorders from the 23 patients receiving a diagnosis of nondissociative psychiatric disorders and from the seven normal control subjects. The discriminant validity of the SCID-D was assessed for total score, presence or absence of a dissociative disorder, and specific dissociative symptoms.

The general data-analytic strategy consisted of two phases. First, a one-way analysis of variance was conducted in order to determine whether there were overall group differences in SCID-D scores at or beyond the conventional $p=0.05$ level of statistical significance. Since a very high level of statistical significance ($p<0.0001$) was always achieved, specific comparisons were made: patients with dissociative disorders versus those with nondissociative psychiatric disorders, patients with dissociative disorders versus normal control subjects, and patients with nondissociative psychiatric disorders versus normal control subjects. The method of Tukey (27) was applied in the standard manner, which holds the experimentwise error rate at the conventional 0.05 level, based on the empirical rationale of Petrinovich and Hardyck (28).

Whether the results were based on total SCID-D scores or any of the five dissociative symptom scores, the trend was always for patients with dissociative disorders to have the highest scores (most pathology), for normal control subjects to have the lowest scores, and for patients with nondissociative psychiatric disorders to have intermediate scores. Also, there was almost no overlapping of total SCID-D scores among the three groups. This also tended to be true, although not as strikingly, for each of the five symptoms. Specifically, each of the three group comparisons (patients with dissociative disorders versus patients with nondissociative psychiatric disorders, patients with dissociative disorders versus normal control subjects, and patients with nondissociative psychiatric disorders versus normal control subjects) was statistically significant (with experimentwise error controlled at 0.05) for total

**TABLE 2. Symptom Scores on the Structured Clinical Interview for DSM-III-R Dissociative Disorders (SCID-D) for Patients With Dissociative Disorders, Patients With Nondissociative Psychiatric Disorders, and Normal Control Subjects[a]**

| | Patients With Dissociative Disorders (N=18) | | Patients With Nondissociative Psychiatric Disorders (N=23) | | Normal Control Subjects (N=7) | | |
|---|---|---|---|---|---|---|---|
| Symptom[b] | Mean | SD | Mean | SD | Mean | SD | F (df=2, 45) |
| Depersonalization | 3.56 | 0.70 | 2.26 | 1.10 | 1.43 | 0.79 | 16.71[c] |
| Derealization | 2.94 | 1.12 | 1.70 | 0.93 | 1.00 | 0.0 | 14.13[c] |
| Amnesia | 3.56 | 0.86 | 2.30 | 1.15 | 1.14 | 0.38 | 17.77[c] |
| Identity confusion | 3.56 | 0.51 | 1.87 | 1.14 | 1.14 | 0.38 | 27.58[c] |
| Identity alteration | 3.67 | 0.77 | 1.96 | 1.11 | 1.00 | 0.0 | 28.59[c] |
| Total SCID-D score | 17.28 | 2.22 | 10.09 | 4.73 | 5.71 | 1.50 | 32.90[c] |

[a] All group differences were statistically significant. The diagnoses were made by clinicians and were based on *DSM-III-R* criteria.
[b] The intercorrelations among the five symptoms ranged from 0.62 to 0.85 for examiner 1 and 0.57 to 0.84 for examiner 2.
[c] $p<0.0001$.

SCID-D, depersonalization, derealization, amnesia, identity confusion, and identity alteration. These results are detailed in table 2.

## DISCUSSION

The SCID-D is the first instrument designed to allow a trained interviewer to make *DSM-III-R* diagnoses of the five dissociative disorders. The reliability of the SCID-D is comparable to that achieved using similar methods with clinical samples in major diagnostic categories on the SADS (9) and the DIS (10). This preliminary study of the SCID-D was designed to provide a stringent test of differential diagnosis by using subjects with psychiatric diagnoses that share common features with the dissociative disorders (e.g., schizophrenia and depression) in addition to a group of normal control subjects. The SCID-D was able successfully to discriminate individuals with *DSM-III-R* dissociative disorders from these other diagnostic groups as well as from normal control subjects. In addition to providing a diagnosis that confirmed clinicians' diagnosis of a dissociative disorder in all 18 patients, the SCID-D was able to identify seven cases of previously undetected dissociative disorders. Four of these diagnoses were subsequently independently confirmed; for three patients no follow-up data were available. In each of these seven patients both of the SCID-D examiners agreed on the positive SCID-D diagnosis. This critical finding defined the SCID-D instrument as one that appears capable of identifying cases of dissociative disorder that were previously undetected. Given the frequency with which the dissociative disorders have gone undetected, our preliminary results are encouraging and underscore the importance of exploring further the discriminative power of the SCID-D.

Confirming the discriminative strength of the SCID-D, there were no instances of a cluster of severe dissociative symptoms in patients with nondissociative diagnoses. Furthermore, all but two of the 18 patients with dissociative diagnoses had moderate to severe ratings for at least three of the five dissociative symptoms, and most displayed a cluster of four or five moderate to severe symptoms. Two remaining dissociative diagnoses included one of depersonalization disorder with recurrent depersonalization and no other dissociative symptoms and another of dissociative disorder not otherwise specified with two moderate to severe dissociative symptoms. The patients with dissociative disorders tended to suffer from more of the five dissociative symptoms than did patients with other psychiatric disorders, and their symptoms tended to be more severe. Normal control subjects could exhibit any of the five dissociative symptoms but tended to have them in isolation and with much less severity and frequency.

In addition to providing a confirmatory diagnosis based on specific diagnostic criteria, the SCID-D was able to assess the severity of dissociative symptoms in other groups of psychiatric patients. The SCID-D is designed to evaluate the severity of symptoms whether or not the individual meets diagnostic criteria for a dissociative disorder. The systematic assessment of dissociative symptoms using the SCID-D severity ratings may be able to provide additional information about symptom constellations in the dissociative disorders as well as about dissociative symptoms in other psychiatric conditions, such as borderline personality disorder, posttraumatic stress disorder, and substance abuse disorders (2, 3, 5, 14, 29). Such additional information may prove helpful in future investigations of dissociative as well as other types of pathology.

Some possible limitations of this investigation are as follows. 1) The study relied on a relatively small group of subjects and the patients studied were all outpatients. Nonetheless, the outpatient sample may well provide a more stringent test of the reliability of the SCID-D, since outpatients with dissociative disorders often present with more subtle manifestations of their illness. To illuminate further this important nosologic issue, further investigations of the reliability of the SCID-D using an inpatient sample are currently in progress. The achievement of discriminant validity, however, is more difficult with small samples than with larger samples, and the validity results of this preliminary study are therefore considered promising. 2) The clinicians' diagnoses of 15 patients were known to the primary interviewer. However, when the data were subsequently analyzed both with and without these 15 patients the results were not significantly different. 3) The study relied on the co-rating of videotapes rather than a test-retest reliability research design. One potential drawback to videotape reliability studies is the inadvertent cuing of raters (30). To reduce this potential source of bias, no sections of the SCID-D were skipped even when screening questions were answered in a clinically insignificant manner. Furthermore, there is no one-to-one correspondence of individual items to diagnostic criteria on the SCID-D, and single responses are therefore less likely to cue the co-rater. 4) Only two co-raters were available for this study. An expanded study has been undertaken using a test-retest reliability design, blind examiners, and a larger patient sample to explore these issues further. Research is also currently underway to explore more thoroughly the generalizability of these findings by using the SCID-D in a multicenter study with a larger number of subjects and examiners who are blind to patients' diagnoses.

The SCID-D is a new instrument developed to help surmount the difficulty of making a diagnosis of the five dissociative disorders. Preliminary findings indicate acceptable levels of reliability and discriminant validity for this instrument. A uniform diagnostic instrument has not previously been available for use in large-scale epidemiologic or controlled pharmacological studies of the dissociative disorders. The SCID-D shows promise as an instrument for such studies. It provides a system of uniform ratings for individual dissociative symptoms as well as uniform diagnoses of the major dissociative disorders and may, therefore, also have utility in the evaluation of dissociative episodes occurring within nondissociative psychiatric disorders. Further research using the SCID-D will continue to clarify its clinical and research utility.

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## APPENDIX 1. Sample SCID-D Items: Depersonalization

*Past Symptoms/Current Symptoms: Depersonalization*

| | | |
|---|---|---|
| Some people have had experiences that feel very real to them, but are very hard to explain to other people. Now, I am going to ask you about some of these experiences. | | |
| 26. Have you ever felt that you were watching yourself from a point outside of your body, as if you were seeing yourself from a distance (or watching a movie of yourself)? | **Depersonalization**<br>"The symptom of depersonalization involves an alteration in the perception or experience of the self so that the usual sense of one's own reality is temporarily lost or changed. This is manifested by a sensation of self-estrangement or unreality, which may include the feeling that one's extremities have changed in size, or the experience of seeming to perceive oneself from a distance." (*DSM-III*) Often reported by phrases such as "I don't feel like myself," "I look at my hand and wonder to whom it belongs." (Examples are from *The Glossary of Psychoanalytic Terms* [18])<br>DESCRIBE: | ? 1 2 3 4[a] |
| IF YES, ask question 27.<br>IF NO, go to question 28. | | |
| 27. When was that? What was that experience like? How often have you had that experience? | DESCRIBE:<br>**Frequency of depersonalization**<br>?=unclear<br>1=rarely<br>2=occasionally<br>3=frequently<br>4=most of the time<br>5=variable frequency | ? 1 2 3 4[a] |
| 28. Have you ever had the feeling that you were a stranger to yourself?<br>IF YES, ask, When was that? What was that experience like? | DESCRIBE: | ? 1 2 3 4[a] |
| 29. Have you ever felt as if a part of your body or your whole being was foreign to you? | | ? 1 2 3 4[a] |

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[a] ?=inadequate information, 1=absent, 2=subthreshold, 3=threshold (present), 4=inconsistent information.

## APPENDIX 2. SCID-D Diagnostic Score Sheet for Depersonalization Disorder

| | SCID-D Items | Yes | No |
|---|---|---|---|
| *DSM-III-R* criterion A for depersonalization disorder:<br>Persistent or recurrent experiences of depersonalization as indicated by either 1 or 2: | | ___ | ___ |
| 1. An experience of feeling detached from, and as if one is an outside observer of, one's mental processes or body | | | |
| 2. An experience of feeling like an automaton or as if in a dream | | | |
| SCID-D items supporting criterion A:<br>One of the following in persistent or recurrent episodes | 26–34a, 40 | ___ | ___ |
| 1. An experience of observing one's self, as if one is an outside observer of one's body | 26, 27, 34 | ___ | ___ |
| 2. A sensation of self-estrangement or unreality regarding one's self (may be reported by phrases such as, "I don't feel like myself," "I look at my hand and wonder to whom it belongs") (18) | 28, 29, 32, 35 | ___ | ___ |
| 3. An experience of feeling detached from one's behavior or body | 30, 33 | ___ | ___ |
| 4. Feeling like an automaton; as if one is going through the motions of life; or feeling disconnected from one's behavior | 33, 34, 39 | ___ | ___ |
| *DSM-III-R* criterion B for depersonalization disorder:<br>During the depersonalization experience, reality testing remains intact | | ___ | ___ |
| SCID-D criteria supporting criterion B:<br>Reality testing remains intact, as evidenced by | 25–55 | ___ | ___ |
| 1. During the depersonalization episode, patient experiences body or self "as if" detached or separated. Patient does not believe that self or body have in fact been detached or separated | | ___ | ___ |
| 2. During depersonalization episode, there is no evidence of psychotic thinking | | ___ | ___ |
| *DSM-III-R* criterion C for depersonalization disorder:<br>The depersonalization is sufficiently severe and persistent to cause marked distress | | ___ | ___ |
| SCID-D items supporting criterion C:<br>The presence of both of the following | | | |
| 1. Recurrent or persistent episodes of depersonalization | 27, 34a, 40, 41 | ___ | ___ |
| 2. The depersonalization episode causes marked distress | 46–48 | ___ | ___ |
| *DSM-III-R* criterion D for depersonalization disorder:<br>The depersonalization experience is the predominant disturbance and is not a symptom of another disorder, such as schizophrenia, panic disorder, or agoraphobia without history of panic disorder but with limited symptom attacks of depersonalization, or temporal lobe epilepsy | | | |
| SCID-D items supporting criterion D:<br>The presence of all of the following | | | |
| 1. The depersonalization episode is the predominant disturbance | 55–59 | ___ | ___ |
| 2. The depersonalization episode is not a symptom of another disorder, such as schizophrenia or panic disorder (see SCID-D exclusion criteria) | 55–59 | ___ | ___ |
| 3. The depersonalization episode is not a symptom of temporal lobe epilepsy or other seizure disorder | 50–54 | ___ | ___ |
| 4. Recurrent depersonalization episodes are not initiated by drugs or alcohol | 50–54 | ___ | ___ |

# Assessing Symptom Change in Southeast Asian Refugee Survivors of Mass Violence and Torture

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Toan Truong, Svang Tor, and Ter Yang

*The authors evaluated changes in symptoms and levels of perceived distress of 21 Cambodian, 13 Hmong/Laotian, and 18 Vietnamese patients before and after a 6-month treatment period. Most of the patients improved significantly. Cambodians had the greatest and Hmong/Laotians had the least reductions in depressive symptoms. Although psychological symptoms improved, many somatic symptoms worsened. The authors conclude that refugee survivors of multiple traumata and torture can be aided by psychiatric care. They recommend investigations with larger samples and suitable control groups to further clarify the relative contributions of trauma, diagnosis, and acculturation stress to treatment outcome.*

(Am J Psychiatry 1990; 147:83–88)

Highly traumatized refugee populations number more than ten million worldwide; more than one million refugees (more than 700,000 Indochinese) have resettled in the United States since 1975 (1). Although many members of these populations are at high risk for serious psychiatric disorder, knowledge concerning the psychiatric care of refugee survivors of mass violence and torture is in its infancy (2). Community studies of resettled Indochinese groups in the United States (3, 4) have revealed that they have serious unmet mental health needs. Linguistic and cultural barriers as well as other factors prevent treatment of Indochinese groups. Furthermore, little is known of the course of illness in highly traumatized refugee patients. Few empirical studies are available to guide clinicians as to the most effective posttraumatic therapies (5, 6).

Recognizing the severe mental health needs of Indochinese communities, the U.S. Office of Refugee Resettlement awarded our clinic a national demonstration project grant to conduct a pilot study of the effectiveness of our specialized treatment approach. This study was aimed at observing the symptom response of highly traumatized Indochinese refugee patients to psychiatric intervention over a 6-month period. An additional aim was to demonstrate to Western clinicians inexperienced with Indochinese patients the ability of psychiatric care to ameliorate the overwhelming hopelessness of individuals who have suffered horrific life experiences. Although generalizations from this study's findings are limited, assessing symptom change is a necessary step toward more extensive empirical evaluations of the effectiveness of psychiatric treatment of patients who have experienced severe trauma and torture (2, 5).

## METHOD

### Assessment

The specific aim of this study was to evaluate psychiatric symptom change in three Indochinese ethnic groups treated in a specialized clinic (the Indochinese Psychiatry Clinic) over a 6-month period. All patients in treatment in January 1984 and all new admissions to the clinic over the following 6-month period were included in the study. Of the 79 Indochinese patients who were evaluated or in treatment during this time period, 52 completed the 6-month outcome study. The sociodemographic and diagnostic characteristics of the total sample of 79 patients did not differ substantially from those of the 52 adult patients included in this report. To determine the sociodemographic, family, social, and personal characteristics of these patients, the Life Events and Social History Questionnaire, a standardized interview schedule, was used. This questionnaire was developed by our clinic and is available on request from R.F.M. The Life Events and Social History Questionnaire was also used to survey the number of traumatic events experienced by the patients during the war, during their escape, and in the refugee camps. The questionnaire was administered by the clinic's Indochinese paraprofessional staff under the direct supervision of the research coordinator.

*DSM-III* diagnoses of all patients were made by two psychiatrists with more than 2 years of experience

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treating Indochinese patients. In addition, the presence or absence of posttraumatic stress disorder (PTSD) was evaluated by using the National Institute of Mental Health Diagnostic Interview Schedule (7). The patient's highest level of adaptive functioning during the previous year was evaluated by using *DSM-III* axis V criteria. Finally, all patients were assessed for medical disorders by a primary care physician affiliated with the clinic. We reported on the diagnoses of this group of patients in an earlier paper (8).

All patients included in the study provided informed consent.

Symptom change was measured by using the Indochinese versions of the Hopkins Symptom Checklist-25 (HSCL-25) (9). These were administered to each of the 52 patients at the beginning of the study and after the 6-month treatment period. The patients also received a simple self-rating scale of level of experienced illness before and after treatment.

The HSCL-25 was selected for use in this study because of its extensive use in measuring clinical improvement in U.S. patients undergoing psychotherapy (10) and in assessing clinical improvement in psychiatric symptoms in medical outpatient settings (11–13). The HSCL-25 has also been found to be a reliable and valid measure of symptoms of anxiety and depression in highly traumatized refugee patients (9). The HSCL-25 consists of 10 items for anxiety symptoms and 15 items for depressive symptoms. Each item is scored ordinally along four category responses ranging from no symptoms to extreme symptoms. Responses are summed and divided by the number of answered items to generate an anxiety score, a depression score, and a total score between 1 and 4. A score of 1.75 was established by the originators of the instrument (10, 11) as a positive cutoff point for depression, anxiety, and combined total response. (This cutoff point has been established as valid for U.S. communities and still has to be validated for specific Indochinese communities.) Therefore, a Southeast Asian patient who has a total score of 1.75 (25 items) and/or a depression score of 1.75 (15 items) is likely to be considered "checklist positive," presumptively demonstrating a psychiatric disorder.

Analyses were done by using the Statistical Analysis System (SAS) program (14). Analyses of variance and covariance were carried out in order to compare the ethnic groups. Changes between the beginning of the study and after the 6-month treatment period were compared by using paired t tests. All reported p values are two-tailed.

### *Treatment Approach*

Comprehensive details of our clinic's evaluation and treatment approach have been previously described (15). The clinic is located in a primary care setting. Along with psychotropic medication, we use counseling and social service support specifically designed to address the psychiatric disorders and the unique cultural and social and family dimensions of the Indochinese patient. Patients are usually seen weekly by a professionally led team that includes a psychiatrist, a social worker, and an Indochinese mental health worker.

## RESULTS

The major sociodemographic, psychosocial, and diagnostic characteristics of the three major patient ethnic groups have been presented in an earlier paper (8). The major ethic groups were Cambodian (N=21), Hmong/Laotian (N=13), and Vietnamese (N=18).

The Cambodian patients were the most highly traumatized patient group. They had experienced a mean of 16 trauma events, including three torture events. Five Cambodian patients had major affective disorder alone and 12 had major affective disorder and PTSD. The Hmong/Laotian patients had experienced a mean of 11 major trauma events, including two torture experiences. None of these patients had major affective disorder alone, 11 had major affective disorder and PTSD, and one had PTSD alone. The Vietnamese patients were the clinic's least traumatized patients. They had a mean of two trauma events and no torture experiences. Seven had major affective disorder alone, two had major affective disorder and PTSD, and nine had other psychiatric diagnoses, such as schizophrenia and adjustment reactions.

### *Changes in Symptoms Before and After Treatment*

Table 1 presents the HSCL-25 mean scores for the 10 anxiety items and the 15 depression items by ethnic group. It also presents the results of analyses of covariance comparing the ethnic groups with adjustments for sex, presence or absence of PTSD, number of traumata to self, and all incidents of torture reported. Table 2 presents the HSCL-25 mean scores for the anxiety and depression items by the presence or absence of PTSD. It also presents the results of analyses of covariance comparing the patients with adjustments for sex, ethnicity, number of traumata to self, and all incidents of torture reported.

Cambodian and Hmong/Laotian patients had higher anxiety and depression scores at both the beginning of the study and after the 6-month treatment period than did Vietnamese patients. Patients with PTSD (alone or with other psychiatric diagnoses) had higher HSCL-25 scores than patients without PTSD. Mean change scores did not differ significantly from zero except for the depression scores of Cambodians (see table 1).

The differences between ethnic groups adjusted for other factors were no longer significant except for anxiety score after treatment, where the least squares

TABLE 1. HSCL-25 Anxiety and Depression Scores of 52 Indochinese Psychiatric Patients Before and After Treatment, by Ethnic Group

| Item | Cambodians (N=21) | Hmong/ Laotians (N=13) | Vietnamese (N=18) | Analysis of Variance or Covariance[a] | | |
|---|---|---|---|---|---|---|
| | | | | F | df | p |
| Anxiety score | | | | | | |
| Before treatment | | | | 8.19[b] | 2, 49 | 0.0009[c] |
| Mean | 2.21 | 2.15 | 1.49 | | | |
| SD | 0.70 | 0.64 | 0.40 | | | |
| Least squares mean | 1.86 | 2.17 | 2.03 | 6.08[d] | 6, 45 | <0.0001 |
| After treatment | | | | 10.97[b] | 2, 46 | <0.0001[c] |
| Mean | 2.11 | 2.36 | 1.32 | | | |
| SD | 0.89 | 0.46 | 0.30 | | | |
| Least squares mean | 1.50 | 1.98 | 2.24 | 9.82[d] | 6, 42 | <0.0001[e] |
| Paired difference, before and after treatment | | | | 1.87[b] | 2, 46 | n.s. |
| Mean | 0.09 | −0.21 | 0.16 | | | |
| SD | 0.70 | 0.44 | 0.33 | | | |
| Least squares mean | 0.35 | −0.21 | −0.16 | 1.25[d] | 6, 42 | n.s.[f] |
| Depression score | | | | | | |
| Before treatment | | | | 9.92[b] | 2, 49 | 0.0002[c] |
| Mean | 2.29 | 1.97 | 1.49 | | | |
| SD | 0.69 | 0.50 | 0.40 | | | |
| Least squares mean | 1.91 | 1.78 | 2.06 | 8.84[d] | 6, 45 | <0.0001 |
| After treatment | | | | 6.36[b] | 2, 47 | 0.004[c] |
| Mean | 1.95 | 2.05 | 1.38 | | | |
| SD | 0.73 | 0.55 | 0.35 | | | |
| Least squares mean | 1.56 | 1.73 | 2.08 | 6.00[d] | 6, 43 | <0.0001 |
| Paired difference, before and after treatment | | | | 2.30[b] | 2, 47 | n.s.[g] |
| Mean | 0.32[h] | −0.08 | 0.08 | | | |
| SD | 0.67 | 0.39 | 0.44 | | | |
| Least squares mean | 0.35 | 0.03 | −0.04 | 1.38[d] | 6, 43 | n.s. |

[a] Analyses of covariance compared the ethnic groups with adjustments for sex, presence or absence of PTSD, number of traumata to self, and all incidents of torture reported.

[b] Analysis of variance.

[c] Vietnamese patients' scores significantly different from those of Cambodians and Hmong/Laotians ($p \le 0.05$, Duncan's multiple-range test).

[d] Analysis of covariance.

[e] Cambodian patients' scores significantly different from those of Vietnamese ($p=0.0089$, least squares).

[f] Cambodian patients' scores significantly different from those of the Hmong/Laotians ($p=0.0306$, least squares).

[g] Cambodian patients' scores significantly different from those of the Hmong/Laotians ($p \le 0.05$, Duncan's multiple-range test).

[h] Significantly different from zero ($t=2.19$, $df=20$) ($p<0.05$ by two-tailed paired t test).

means for Cambodians and Vietnamese were different at the 5% level and the paired difference in anxiety scores differed between the Cambodian and the Hmong/Laotian patients (see table 1). The difference between patients with and without PTSD on anxiety and depression scores adjusted for other factors were still significantly different, except for the anxiety scores after treatment (see table 2). Differences in scores before and after treatment were not significant.

Table 3 shows a high correlation between improvement in symptom level and the patients' self-assessment of improvement after the 6-month treatment period. By analysis of variance the linear trend was statistically significant for both the 15 depression items and the 10 anxiety items of the HSCL-25.

### *Changes in Individual Symptoms Before and After Treatment*

Individual symptom items of the HSCL-25 and their changes after 6 months of treatment were evaluated. Figure 1 shows the results for the 21 Cambodian patients. Before treatment, Cambodian patients had a mean score above 1.75 on 22 out of 25 symptoms. The highest scores were for worried, hopeless, and blue. Their mean scores on three symptoms—apathy, suicide, and sexual—were below 1.75. The scores on 19 out of 25 symptoms improved between the beginning of the study and after the 6-month treatment period. In figure 1, a positive delta value indicates improvement in symptoms. Four symptoms showed a greater degree of distress after 6 months of treatment—headache, energy, heart, and tremble. Item by item scores for the Vietnamese and Hmong/Laotian groups and for patients with and without PTSD are not shown but are available from R.F.M. on request.

The mean scores of the Vietnamese patients before and after treatment tended to be under 1.75; these patients had mean scores above 1.75 on only three symptoms—energy, faint, and headache. Decrease in appetite showed the greatest worsening over the 6-month period.

**TABLE 2. HSCL-25 Anxiety and Depression Scores of 52 Indochinese Psychiatric Patients Before and After Treatment, by Diagnosis of Posttraumatic Stress Disorder (PTSD)**

| | PTSD Diagnosis | | Analysis of Variance or Covariance[a] | | |
|---|---|---|---|---|---|
| Item | Yes (N=26) | No (N=26) | F | df | p |
| Anxiety score | | | | | |
| Before treatment | | | 18.58[b] | 1, 50 | <0.0001 |
| Mean | 2.30 | 1.60 | | | |
| SD | 0.58 | 0.58 | | | |
| Least squares mean | 2.17 | 1.72 | 7.34[c] | 5, 46 | <0.0001[d] |
| After treatment | | | 20.28[b] | 1, 47 | <0.0001 |
| Mean | 2.34 | 1.51 | | | |
| SD | 0.66 | 0.63 | | | |
| Least squares mean | 2.11 | 1.73 | 9.15[c] | 5, 43 | <0.0001 |
| Paired difference, before and after treatment | | | 0.80[b] | 1, 47 | n.s. |
| Mean | −0.04 | 0.10 | | | |
| SD | 0.58 | 0.52 | | | |
| Least squares mean | 0.08 | −0.01 | 0.79[c] | 5, 43 | n.s. |
| Depression score | | | | | |
| Before treatment | | | 17.65[b] | 1, 50 | <0.0001 |
| Mean | 2.26 | 1.60 | | | |
| SD | 0.57 | 0.56 | | | |
| Least squares mean | 2.18 | 1.68 | 10.84[c] | 5, 46 | <0.0001[e] |
| After treatment | | | 25.51[b] | 1, 48 | <0.0001 |
| Mean | 2.17 | 1.42 | | | |
| SD | 0.58 | 0.46 | | | |
| Least squares mean | 2.10 | 1.48 | 6.70[c] | 5, 44 | <0.0001[f] |
| Paired difference, before and after treatment | | | 0.38[b] | 1, 48 | n.s. |
| Mean | 0.08 | 0.18 | | | |
| SD | 0.53 | 0.57 | | | |
| Least squares mean | 0.07 | 0.19 | 1.30[c] | 5, 44 | n.s. |

[a] Analyses of covariance compared the patients with adjustments for sex, ethnicity, number of traumata to self, and all incidents of torture reported.

[b] Analysis of variance.

[c] Analysis of covariance.

[d] Difference between patients with and without PTSD was significant (p=0.0229, least squares).

[e] Difference between patients with and without PTSD was significant (p=0.0048, least squares).

[f] Difference between patients with and without PTSD was significant (p=0.0032, least squares).

**TABLE 3. Relationship Between HSCL-25 Anxiety and Depression Scores and Level of Self-Rated Improvement in 49 Indochinese Psychiatric Patients After Treatment[a]**

| | Self-Rating | | | Analysis of Variance | | | Linear Contrast | |
|---|---|---|---|---|---|---|---|---|
| Measure | Unimproved (N=14) | Moderately Improved (N=19) | Very Improved (N=16) | F | df | p | F | p |
| Mean anxiety score | 2.44 | 1.92 | 1.46 | 8.17 | 2, 46 | 0.0009 | 16.33 | 0.0002 |
| Mean depression score | 2.16 | 1.88 | 1.37 | 7.71 | 2, 46 | 0.001 | 14.66 | 0.0004 |

[a] Three patients did not rate themselves.

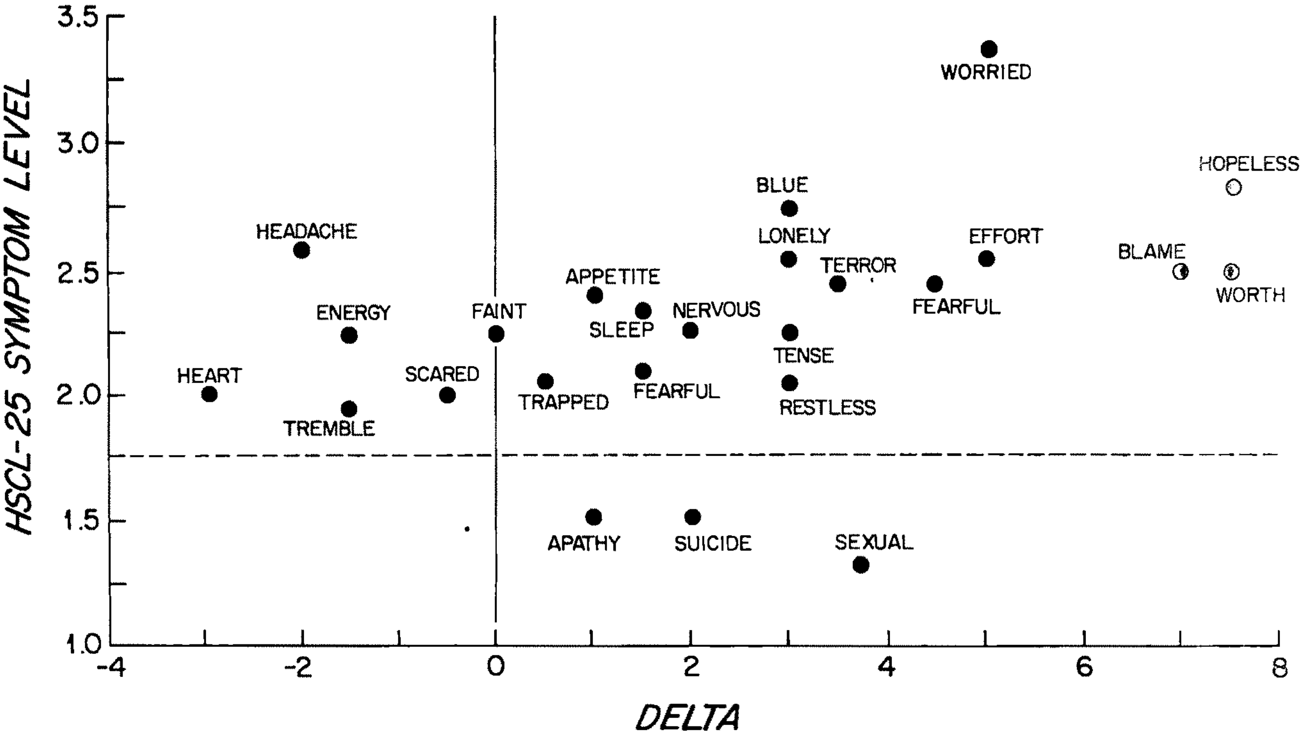
Before treatment, the mean score of the Hmong/Laotian patients was 1.75 or higher on 18 items. The scores of these patients improved on only six symptom items of the HSCL-25—effort, worried, energy, appetite, sexual, and sleep. In contrast, these patients' scores on 18 symptoms worsened; worth (feelings of worthlessness) showed the greatest worsening.

The patients with PTSD had a score above 1.75 on all but three symptoms—suicide, apathy, and sexual—before treatment. These patients showed the greatest improvement in the symptoms of effort, worried, and terror and the greatest worsening in trembling and scared.

## DISCUSSION

Few empirical studies exist on the outcome of psychiatric treatment of survivors of mass violence and torture. Research on the treatment of these patients and their problems is extremely difficult because of many complex scientific and political reasons (2, 5).

**FIGURE 1. Change in Mean HSCL-25 Symptom Scores of 21 Cambodian Psychiatric Patients Before and After Treatment[a]**



[a] Delta=mean symptom score before treatment minus mean symptom score after treatment.

A lack of resources and organizational, cultural, linguistic, and community barriers—including limited psychiatric expertise in caring for individuals with catastrophic life experiences—further prevent these patients from entering treatment and establishing a therapeutic relationship (16).

This study reveals that in a culturally sensitive psychiatric setting:

1. Cambodian patients had modest improvements in depressive symptoms over a 6-month period.
2. Depressive symptoms were more responsive to treatment than were anxiety and somatic symptoms.
3. A high correlation existed between self-report of improvement in level of illness and symptom reduction.

The dramatic improvement of many of the clinic's Cambodian patients is encouraging because it shows that the extreme feelings of hopelessness and worthlessness, which are so common to these patients, are amenable to treatment. The type and severity of the symptoms, revealed by the HSCL-25 scores of the clinic's Cambodian patients before treatment, are consistent with a highly traumatized patient group suffering from major affective disorder and PTSD. The findings after the 6-month treatment period indicate that although most somatic symptoms (especially "headaches") worsen over time, many psychological symptoms improve. This improvement in psychological symptoms, when combined with improved "effort," has been found to be associated with better social functioning (8).

The low number of symptoms of the Vietnamese patients on the HSCL-25 is consistent with their limited history of trauma and their primary psychiatric diagnoses. Many Vietnamese in the clinic's caseload have schizophrenic disorders. The Vietnamese community in the region has access to a well-organized system of health care that includes many Vietnamese primary care physicians. In general, only "psychotic" individuals are referred out of this community for specialized treatment elsewhere. These referrals usually consist of single, isolated, psychotic young men without family in the United States.

The study's finding of the worsening of most symptoms for the clinic's Hmong/Laotian was troublesome. Symptoms of both anxiety and depression worsened in this group. Closer clinical inspection of these patients yielded a number of observations. Like Cambodians they are a highly traumatized group. However, unlike the Khmer of Cambodia, the Hmong of Laos are nonliterate tribal villagers who may be more reluctant to accept psychological counseling because of the greater meaning they give to physical complaints. Second, unknown to us at the time we conducted this study, many Hmong/Laotians were found to have chronic problems with substance abuse in addition to PTSD and depression. Finally, the finding that their feelings of self-worth worsened more than any other item on the

HSCL-25 is consistent with their community's view that the Hmong/Laotians are experiencing greater difficulty and prejudice in their adjustment to U.S. society than other Indochinese groups.

Analysis of covariance could not determine the impact of the diagnosis of PTSD on symptom change because of the small sample size and the skewed ethnic distribution of this diagnosis. However, the stability of total anxiety scores and the worsening primarily of somatic symptoms compared with psychological symptoms such as depression may reflect both the natural history of PTSD and the continued stress associated with acculturation (17, 18). A treatment study with a much larger sample could demonstrate the relative contribution of traumatic events (type and number), diagnosis, and acculturation stress to the severity of presenting symptoms as well as their responsiveness to treatment over time.

Finally, this study's empirical demonstration of improvement in the depressive symptoms and psychological well-being of tortured and traumatized refugee patients is a very optimistic finding for refugee patients and their Western providers of care. These findings should help support the effort of clinicians who often feel overwhelmed and hopeless about their ability to treat individuals who have suffered horrific life experiences (19). These results also suggest that although treatment can be helpful, many symptoms may in fact worsen or not improve. The etiology and proper treatment of those symptoms which may be chronic and are refractory to currently available interventions must be determined through further investigations (20).

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# Psychiatric Diagnosis Before Serological Testing for the Human Immunodeficiency Virus

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*To identify the diagnostic characteristics and counseling needs of individuals at risk for acquired immune deficiency syndrome (AIDS), standardized* DSM-III-R *diagnoses were given to 207 physically asymptomatic adults when they sought serological testing for the human immunodeficiency virus (HIV). The subjects had high lifetime rates of mood disorders. Even after the 20 subjects with intravenous drug use as a risk factor were eliminated, lifetime rates of nonalcohol substance dependence were also high. These findings suggest that even before they are notified of HIV test results, many individuals at perceived risk for AIDS may be vulnerable to future depression and nonintravenous drug abuse.*

(Am J Psychiatry 1990; 147:89–93)

Since sensitive and specific serological assays for the human immunodeficiency virus (HIV) (1) have become widely available, individuals at perceived risk for infection have been voluntarily tested. However, no studies have reported the psychiatric diagnoses of these individuals before they were notified of their test results. Documenting the types and rates of psychopathology in this population by means of standardized clinical ratings (2) would help determine whether these subjects are especially vulnerable to future psychiatric illness.

It has been found that individuals who know that they are HIV positive are at increased risk for distress (3–6) and that individuals with acquired immune deficiency syndrome (AIDS) are at increased risk for suicide (7). However, there are reasons to suspect that even before knowledge of their HIV infection, individuals in major risk groups may have a greater prevalence of psychopathology. Intravenous drug use has been associated with other psychiatric disorders (8), and homosexual men have been reported to have high rates of bipolar mood disorder and alcoholism (9). In addition, with the advent of the AIDS epidemic, clinicians have noted that persons at risk who have not undergone serological testing suffer the adverse psychological consequences of living with the fear that they will acquire this stigmatizing and ultimately fatal infection (10, 11, and unpublished 1987 paper by S. Tross et al.).

There are some dangers, however, in confusing psychological distress and psychopathology. These two may have quite different diagnostic and prognostic implications and may have different counseling, psychotherapeutic, and psychopharmacological requirements (10, 12, 13). Moreover, in the absence of standardized diagnostic ratings or in the interpretation of diagnostic ratings in small, select samples (14), there is danger in assuming that at-risk individuals represent a psychiatrically morbid population, an assumption that might result from and also foster prejudice against at-risk groups.

To address these issues, we determined the *DSM-III-R* axis I psychiatric diagnoses of a group of physically asymptomatic adults 2 weeks before they were notified of the results of their HIV tests. We were aware that these subjects—although they were sociodemographically heterogeneous and represented major risk factors for HIV—would unavoidably constitute a select sample because of their interest in voluntary HIV testing and their willingness to participate in a research protocol. Nonetheless, in the absence of any currently available data, the rates of psychopathology in these subjects before notification of their HIV status would provide a crucial first step for future comparison with results of other studies as research continues to identify the psychotherapeutic needs of individuals at risk for AIDS.

## METHOD

As part of a longitudinal study of psychobehavioral responses to HIV antibody testing (15), free and confidential testing with standardized counseling (13) was offered to adults at risk for AIDS: homosexual/bisex-

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ual men, intravenous drug users, and heterosexual partners of those with known or suspected HIV infection. Most subjects (78%, N=161) were recruited through weekly newspaper advertisements; the remaining 22% (N=46) learned of the study primarily from other subjects, from clinicians in metropolitan medical clinics, or from drug rehabilitation programs whose directors had been informed of the study through personal contact by the investigators or a written description of the study that we had distributed. No subjects were referred for the express purpose of psychiatric or medical care, and our promotional material made it clear that we would not provide such care.

The subjects' psychiatric diagnoses were made at entry into the study in private offices located in a residential apartment building. Reliability of the ratings on the Structured Clinical Interview for DSM-III-R (SCID) (2) was achieved and sustained through supervision by the project director (L.B.J.), who was trained in administering and scoring the SCID while he was a research Fellow with the authors of the instrument. The project director trained the other six clinical raters: an experienced psychiatric nurse and five advanced psychology graduate students. Reliability was determined following training; assessments were reevaluated periodically to guard against drift. One of every seven diagnostic interviews was conducted in the presence of a nonparticipating corater. Chance-corrected interrater reliability (kappa) on the SCID ranged upward from 0.80 for the diagnosis of lifetime major depression. In detecting the presence of any diagnosis among the test cases, perfect reliability (kappa=1.0) was achieved.

To determine how rates of axis I psychopathology before notification of HIV status compared with rates after notification of positive results but before development of AIDS, SCID diagnoses were also given to 24 physically asymptomatic subjects who had previously been tested and informed elsewhere that they were HIV positive and who had been recruited into the longitudinal psychobehavioral study by similar methods. No identically obtained data are yet available on how previously untested and previously tested subjects compared diagnostically with community populations. However, in the multisite Epidemiologic Catchment Area program, the Diagnostic Interview Schedule (DIS) was administered to more than 10,000 subjects selected to represent a community sample (16–19). Although the DIS was administered by nonclinicians and relies heavily on subject self-report whereas the SCID incorporates a professional's clinical judgment, we chose the Epidemiologic Catchment Area study for comparison because its data currently provide the most comprehensive documented rates of psychiatric disorders in community samples, because its published findings provide for some sex and age comparisons, because less extensive control groups would be subject to marked selection bias, and because the potential differences between the DIS and the SCID (20) would not preclude a rough comparison of current and lifetime prevalence of axis I disorders.

The study subjects included 150 men and 57 women whose mean±SD age was 33.6±10.2 years (range=19.8–66.0). One hundred fifty-nine of the subjects were white, 18 black, 22 Hispanic, four Asian, and four other. The median annual income was in the $15,000–$30,000 range (six had no income and 20 earned over $50,000 per year). Sixty-three subjects had some postgraduate education, 53 a college degree, 69 some college credits, and 17 a high school diploma; five had not completed high school.

## RESULTS

The overall rate of positive HIV test results was 16%: 31 of the 134 homosexual/bisexual men, two of the 20 intravenous drug users, two of the 70 whose heterosexual partners were at known or suspected risk (prostitutes, intravenous drug users, persons with multiple partners), and none of the six subjects (two female and four male) who were self-referred because they perceived a risk but who disclosed only remote risk factors (for example, a brief extramarital affair) tested positive. The men had a 21% rate of positive test results, compared to a 5% rate among the women ($\chi^2=6.1$, df=1, p=0.01), with most of the men (89%, N=134) having homosexual risk factors.

Table 1 presents the rates of current (within the last month) and lifetime SCID diagnoses of the subjects who sought HIV testing in our research setting. Included in the tabulation of "any axis I disorder" were five eating, three adjustment, three somatoform, and two posttraumatic stress disorders. Table 1 also presents rates of current (within the last month) and lifetime major DIS diagnoses in community samples (18, 19). Rates for men and women are reported separately if available. Where a range is given, it is because different rates were reported from three Epidemiologic Catchment Area sites.

Table 1 indicates that rates of any current axis I disorder were only slightly higher in the subjects who sought HIV serological tests than in the community samples. However, rates of current mood disorders in both the male and female subjects and of current alcohol and other nonintravenous substance dependence in the female subjects were notably higher. Comparison of lifetime rates is even more striking, showing much higher rates of mood disorders and nonalcohol substance dependence in both the male and female subjects and of alcohol dependence in the female subjects. Consequently, the study subjects' rates of any lifetime axis I disorder were roughly double the lifetime rates in the Epidemiologic Catchment Area samples.

The 35 subjects later found to have positive HIV test results were no more likely to have axis I diagnoses than the 172 subjects whose test results were negative. Rates for any current axis I disorder were not statisti-

TABLE 1. *DSM-III-R* Axis I Diagnoses of 150 Male and 57 Female At-Risk Subjects Before HIV Serological Testing and of Epidemiologic Catchment Area Community Samples

| | Subjects With Current Disorder | | | | | | Subjects With Lifetime Disorder | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | At-Risk Subjects | | | | Epidemiologic Catchment Area Community Samples[a] (%) | | At-Risk Subjects | | | | Epidemiologic Catchment Area Community Samples[b] (%) | |
| | Male | | Female | | | | Male | | Female | | | |
| Diagnosis | N | % | N | % | Male | Female | N | % | N | % | Male | Female |
| Mood disorders | 21 | 14.0 | 8 | 14.0 | 3.5 | 6.6 | 64 | 42.7 | 28 | 49.1 | 6.1–9.5 | |
| Major depression | 7 | 4.7 | 6 | 10.5 | 1.6 | 2.9 | 43 | 28.7 | 25 | 43.9 | 2.3–4.4 | 4.9–8.7 |
| Dysthymic disorder | 11 | 7.3 | 2 | 3.5 | 2.2 | 4.2 | — | — | — | — | 1.2–2.6 | 2.9–3.7 |
| Bipolar disorder | 0 | 0.0 | 0 | 0.0 | 0.3 | 0.4 | 4 | 2.7 | 0 | 0.0 | 0.8–1.1 | 0.5–1.3 |
| Substance dependence | | | | | | | | | | | | |
| Alcohol | 5 | 3.3 | 3 | 5.3 | 5.0 | 0.9 | 30 | 20.0 | 11 | 19.3 | 19.1–28.9 | 4.2–4.8 |
| Nonalcohol, nonintravenous[c] | 6 | 4.4 | 3 | 6.0 | 1.8 | 0.7 | 35 | 25.5 | 18 | 36.0 | 6.5–7.4 | 3.8–5.1 |
| Anxiety disorders | 10 | 6.7 | 5 | 8.8 | 4.7 | 9.7 | 19 | 12.7 | 9 | 15.8 | 10.4–25.1 | |
| Any axis I disorder | 37 | 24.7 | 17 | 29.8 | 14.0 | 16.6 | 90 | 60.0 | 41 | 71.9 | 30.6–37.0 | 25.7–36.7 |

[a] See reference 19.
[b] See reference 18.
[c] Data for 137 male and 50 female subjects remaining after 13 male and seven female subjects with an intravenous drug use risk factor were eliminated from the analysis.

cally different between the two groups (38.2% and 23.7%, respectively; $\chi^2=2.2$, df=1, p=0.14), nor was there a difference in lifetime prevalence (67.6% and 62.4%, respectively).

The group of 24 subjects whose positive HIV test results were known at the time of the evaluation was composed of six exclusively homosexual men, 14 bisexual men, two heterosexual men who were intravenous drug users, and two women who had been infected by HIV-positive heterosexual partners. The 20 homosexual/bisexual men in this group did not differ significantly in mean age, racial distribution, median annual income, and level of education from the 31 homosexual/bisexual men who later had positive test results or the 103 homosexual/bisexual men who were found to be HIV negative.

Table 2 shows the types and rates of psychopathology among these three homosexual/bisexual groups and among the most appropriate available comparison groups from the Epidemiologic Catchment Area community samples. The findings indicate that the homosexual/bisexual men who sought HIV serological testing in response to our promotional material had especially high rates of current and lifetime mood disorders and of lifetime nonalcohol substance dependence. Table 2 also shows that even before notification of HIV test results, homosexual/bisexual subjects who turned out to be HIV positive tended to have higher rates of current major axis I disorders than those who turned out to be HIV negative (for example, mood disorders, 22.6% versus 10.7%; alcohol dependence, 9.7% versus 1.9%). When we compared rates of any axis I disorder for those who later tested HIV positive (38.7%) and those who tested HIV negative (20.4%), the difference approached statistical significance ($\chi^2=3.4$, df=1, p=0.07).

## DISCUSSION

The major objective of this study was to determine the rates of psychopathology in a heterogeneous group of physically asymptomatic adults at perceived risk for AIDS who were voluntarily seeking the HIV antibody test. This information would provide a crucial step toward identifying the psychiatric vulnerability of these individuals and their specific psychotherapeutic requirements. In this regard, our findings are particularly helpful. High lifetime rates of mood disorders were found in both men (42.7%) and women (49.1%), roughly seven times the rates in age-matched community samples. It is not yet known whether individuals with histories of mood disorders are more susceptible to depression in response to living with the risk of infection, to being notified of positive HIV test results, to developing AIDS, or to the direct neurotropic effects of HIV (21, 22). However, it has been shown that suicide rates in patients with AIDS are remarkably high (7) and that there is an association between perceived self-efficacy and practicing safer sex (23). Therefore, in terms of reducing future psychiatric morbidity and risk behavior, our findings suggest that presentation for HIV testing may provide an opportune time to identify individuals with histories of mood disorders and then to educate this large subgroup about indications for psychiatric treatment.

Also noteworthy were the high lifetime rates of dependence on nonintravenous substances for both the men and the women at perceived risk for AIDS. Even after the intravenous drug users were eliminated from the analysis, about 20% of our sample had a history of alcohol dependence and about 30% had a history of dependence on other drugs (marijuana, cocaine, other stimulants, etc.). This finding is helpful in alerting clinicians to address, during HIV counseling, the adverse

**TABLE 2.** ***DSM-III-R*** **Axis I Diagnoses of 103 HIV-Negative and 31 HIV-Positive Homosexual/Bisexual Men Before Serological Testing, of 20 Physically Asymptomatic Homosexual/Bisexual Men Known To Be HIV Positive, and of Epidemiologic Catchment Area Community Samples**

| | Subjects With Current Disorder | | | | | | | Subjects With Lifetime Disorder | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | HIV Negative | | HIV Positive | | Known HIV Positive | | Epidemiologic Catchment Area Community Samples[a] (%) | HIV Negative | | HIV Positive | | Known HIV Positive | | Epidemiologic Catchment Area Community Samples[b] (%) |
| Diagnosis | N | % | N | % | N | % | | N | % | N | % | N | % | |
| Mood disorders | 11 | 10.7 | 7 | 22.6 | 4 | 20.0 | 4.5[c] | 43 | 41.7 | 16 | 51.6 | 6 | 30.0 | 6.1–9.5[d] |
| Major depression | 5 | 4.9 | 2 | 6.5 | 0 | 0.0 | 2.2[c] | 31 | 30.1 | 10 | 32.3 | 3 | 15.0 | 2.3–4.4[e]<br>7.5–10.4[f] |
| Dysthymic disorder | 5 | 4.9 | 3 | 9.7 | 4 | 20.0 | 2.8[c] | — | — | — | — | — | — | 1.2–2.6[e]<br>2.9–4.4[f] |
| Bipolar disorder | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 | 0.5[c] | 2 | 1.9 | 2 | 6.5 | 0 | 0.0 | 0.8–1.1[e]<br>1.5–1.7[f] |
| Substance dependence | | | | | | | | | | | | | | |
| Alcohol | 2 | 1.9 | 3 | 9.7 | 0 | 0.0 | 6.2[c] | 20 | 19.4 | 8 | 25.8 | 3 | 15.0 | 19.1–28.9[e]<br>14.8–21.0[f] |
| Nonalcohol, nonintravenous[g] | 4 | 4.3 | 2 | 6.5 | 0 | 0.0 | 2.3[c] | 21 | 22.3 | 13 | 41.9 | 3 | 15.8 | 6.5–7.4[e]<br>7.2–9.0[f] |
| Anxiety disorders | 6 | 5.8 | 3 | 9.7 | 0 | 0.0 | 4.7[c] | 10 | 9.7 | 6 | 19.4 | 0 | 0.0 | 10.4–25.1[d] |
| Any axis I disorder | 21 | 20.4 | 12 | 38.7 | 4 | 20.0 | 15.4[c] | 58 | 56.3 | 21 | 67.7 | 8 | 40.0 | 30.6–37.0[e]<br>35.8–43.8[f] |

[a] See reference 19.
[b] See reference 18.
[c] Male subjects only, ages 25–44 years.
[d] Male and female subjects, all ages.
[e] Male subjects only, all ages.
[f] Male and female subjects, ages 25–44 years.
[g] Data for 94 HIV-negative, 31 HIV-positive, and 19 known HIV-positive subjects remaining after nine HIV-negative subjects and one known HIV-positive subject with intravenous drug use as a risk factor were eliminated.

psychosocial and possibly immunological (24) effects of future substance dependence in this large, vulnerable subgroup. This finding is also helpful from a public health perspective, because studies have found that homosexual men who combine use of alcohol or drugs with sex are more likely to engage in high-risk sexual behavior (23).

Although the high lifetime rates of mood and substance dependence disorders warrant emphasis, it must not go unstated that most (more than 70%) of our subjects did not have current *DSM-III-R* axis I psychopathology. In fact, their rates of any axis I disorder were not substantially different from the rates found in the Epidemiologic Catchment Area community samples. This finding may help reduce any prejudicial and stigmatizing views that physically asymptomatic individuals at risk for AIDS represent a psychiatrically morbid population.

Two cautions are necessary in interpreting our findings. First, every sample of individuals at risk for HIV infection is subject to its own selection biases. It could be argued that our group of subjects was biased toward psychiatric health because of the relatively small percentage of intravenous drug users (9.7%) and because the subjects were primarily recruited by newspaper advertising, were aware of their risk factors, and were willing to be serologically tested and participate in a rather burdensome longitudinal study. On the other hand, it could be argued that this group was biased toward psychiatric morbidity because the subjects expected more support than is provided at alternative testing sites or from clinics and private physicians. Unavoidably, possible selection bias cannot be ascertained until future diagnostic studies are conducted elsewhere.

The second caution, related to the first, regards interpreting the comparison with the Epidemiologic Catchment Area data, which were collected with different diagnostic methods, which provide limited sociodemographic information, and which have lifetime prevalence rates that are suspiciously low, since they are only marginally greater than the current prevalence rates. Nevertheless, considering the racial, economic, and educational heterogeneity of our sample, the Epidemiologic Catchment Area findings provide at least a rough approximation of how our subjects who sought HIV testing compare diagnostically with community populations.

Although the primary objective of our study was to document rates of psychopathology before subjects were notified of their HIV status, two additional preliminary findings warrant future research. First is the trend ($p=0.07$) toward higher rates of current major axis I disorders in homosexual/bisexual men who later tested HIV positive than in those who later tested HIV negative. Perhaps those who were later found to be HIV positive knew at some level that they were more likely to be infected and this knowledge affected their current mood—a possibility suggested by a comparable rate of current mood disorder (20%) in our physically asymptomatic subjects who had already been informed about their positive test results. Another possibility, supported by studies showing a relationship between homosexual risk behavior and both self-esteem and alcohol or nonintravenous drug use (23), is that current axis I psychopathology contributed to the acquisition of HIV. Given the public health import, further investigation of this issue is urgently needed.

A second preliminary result warranting future study is that our sample of homosexual/bisexual men who already knew that they had positive HIV test results did not have high rates of psychopathology. In fact, those who already knew that they were HIV positive had considerably lower rates of any current axis I disorder than those who found out later that their results were positive (20.0% and 38.7%, respectively). Small sample size and possible selection bias preclude definitive conclusions, but the findings suggest the importance of distinguishing current psychopathology from distress over knowing about a positive HIV test result. For example, Atkinson et al. (14) found elevated rates of anxiety and mood and substance dependence disorders in 17 asymptomatic homosexual men who were diagnostically evaluated by the DIS a year after they had been notified that they were HIV positive, but the retrospective design precluded determining whether the psychopathology existed before HIV testing or could be attributed to the effects of living with the threat of an ultimately fatal infection. Until further systematic prospective diagnostic studies are conducted, it may be a disservice to suggest that knowledge that one is HIV positive itself induces major axis I psychopathology. Rather, our findings indicate that individuals at risk for AIDS before testing have high lifetime rates of mood and substance dependence disorders that should be addressed during HIV counseling.

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# Neuropsychiatric Manifestations of Altered Thyroid State

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*The authors assessed the mood and cognitive effects of sequential $T_4$, $T_3$, and withdrawal of thyroid hormone replacement on 25 patients who had had thyroidectomies for thyroid cancer. The patients experienced increased sadness and anxiety when they were without medication, but no significant difference in mood was noted between $T_4$ and $T_3$. The patients who experienced increased affective symptoms when not taking medication were more likely to have histories of affective illness or mood lability.*

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There is a vast literature on the relationship between thyroid function and neuropsychiatric symptoms. Clinical studies attempting to clarify this relationship have evaluated neuropsychiatric symptoms in patients with thyroid disease (1–4), thyroid functioning in psychiatric patients (5, 6), triiodothyronine ($T_3$) potentiation of antidepressant efficacy (7, 8), and the effects of thyrotropin-releasing hormone (TRH) on depression (9). Psychiatric symptoms are reported to be a common clinical complication of thyroid disorders (1). In particular, hypothyroidism has frequently been described as accompanied by depressive symptoms (1). Whybrow and Ferrell (1) reported that in a group of seven hypothyroid patients the predominant affective disturbance was a marked depression of mood. Jain (2) assessed 30 consecutive patients diagnosed as hypothyroid and judged 13 patients to be clinically depressed. In addition, patients who are hypothyroid have been reported to suffer from impairment of cognitive functions, such as recent memory, concentration, and simple calculations (1, 2, 4).

Conversely, it has been reported that some psychiatric patients have abnormal results on thyroid function tests. Gold et al. (5) reported that in 100 consecutive patients referred to a neuropsychiatric evaluation and research unit with complaints of depression and/or anergia, nine patients had low $T_3$ uptake, a low thyroxine ($T_4$) level, a high basal thyrotropin (TSH) level, or a change in TSH greater than 35 μIU/ml in response to TRH stimulation. Five of these patients were diagnosed as suffering from major depression, and the other four had atypical or minor depression. Loosen (10) has reported that the TSH response to exogenously administered TRH is blunted in approximately 25% of patients with major depression.

The association between depression and hypothyroidism is consistent with the hypothesis that increases in thyroid hormone levels accelerate recovery and decreases in thyroid hormone levels interfere with recovery in patients with major depression (11). However, studies have shown that most treatments which are effective in manic-depressive illness are associated with significant decreases in thyroid hormone levels (12). Responders to lithium (R.T. Joffe, unpublished data), carbamazepine (13), and possibly ECT (14) have a significantly greater decrease in thyroid hormone levels than do nonresponders. These observations led to Joffe et al.'s hypothesis (12) that decreases in $T_4$, with consequent decreases in cerebral thyroid hormone concentrations, are required for successful treatment in depression. This hypothesis is based on a variety of evidence suggesting that cerebral $T_4$ and $T_3$ are primarily derived from plasma $T_4$ and that, therefore, exogenous $T_4$ and $T_3$ would have different effects on cerebral thyroid concentrations and hence cerebral function (e.g., mood or cognition). If such differences could be identified, it could advance our understanding of the role of thyroid hormones in neuropsychiatric, particularly affective, illness and its treatments. In this study we investigated mood and cognitive changes in thyroidectomized patients receiving $T_4$, $T_3$, and no thyroid hormone.

## METHOD

The subjects were 25 patients who had had thyroidectomies for thyroid cancer and who, in preparation for thyroid scans, received sequentially $T_4$, $T_3$, and no thyroid hormone replacement. They ranged in age from 21 to 62 years; 19 were female, and six were

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male. Most of the patients were in good health except for their thyroid conditions. Two patients suffered from hypertension, one had hypoparathyroidism, one had polymyositis, and one displayed decreased strength in her extremities because of vertebral/spinal cord pathology. One patient had a current diagnosis of major depression. Nine patients had past histories of psychiatric illness: five had had major depression, and one each had had bipolar II disorder, adjustment disorder-depressed mood, organic delusional syndrome, and dysthymic disorder.

The patients received maintenance $T_4$ and were then changed to $T_3$ for 4 weeks. The $T_3$ was then discontinued, and the subjects received no thyroid medication for approximately two and a half weeks. When the patients were receiving maintenance $T_4$, the dose was titrated to an amount that was sufficient to suppress the TSH to below 1.0 μIU/ml according to an ultrasensitive assay. When the patients were switched to $T_3$, the dose was usually quartered. For example, a patient who was receiving 200 μg/day of $T_4$ would be given 50 μg/day of $T_3$ (25 μg b.i.d).

Both cross-sectional and longitudinal assessments were performed. Tests were administered on three occasions: just before discontinuation of $T_4$, during the fourth week of $T_3$ replacement, and during the third week without thyroid hormone replacement. Mood assessment included administration of the Beck Depression Inventory (15), the Spielberger State Anxiety Scale (16), and the SCL-90 (17). The Beck and the Spielberger inventories are 21- and 20-item questionnaires that provide total depression and anxiety scores, respectively. The SCL-90 is a self-report inventory that measures different dimensions of psychopathology, including depression, anxiety, somatization, and anger-hostility. The cognitive tests included a standardized mental status test called the Cognitive Capacity Screening Examination (18) and the digit-symbol subtest of the WAIS (19). The Cognitive Capacity Screening Examination is a 30-point test that examines a variety of cognitive functions, such as orientation, memory, calculations, and abstraction. The WAIS digit-symbol subtest consists of rows of blank squares, each paired with one of nine randomly assigned nonsense symbols. At the top of the page is a key that pairs each nonsense symbol with a number from one to nine. The patient is allowed 90 seconds to fill in the blank squares with the appropriate numbers. In addition, a semistructured interview of lifetime psychiatric history, the modified Schedule for Affective Disorders and Schizophrenia—Lifetime Version (SADS-L) (20), was administered at the time of the first assessment. The patients used visual analogue scales to rate themselves daily on mood, anxiety, physical comfort, mental tranquility, concentration, energy level, and global assessment.

Within several days of each of the three assessments, while the patients were in a nonfasting state, venous blood samples were drawn for measurement of $T_4$, free $T_4$, $T_3$, TSH, and thyroxine-binding globulin. All blood samples were drawn between 8:00 a.m. and 5:00 p.m. The TSH was measured by means of radioimmunoassay. The lower limit of sensitivity of the assay is 0.1 μIU/ml. The intra-assay coefficients of variation for TSH were 5% at 1.9 μIU/ml, 10% at 9.9 μIU/ml, and 10% at 22.8 μIU/ml.

Analysis of variance with repeated measures (ANOVA) was performed for each psychometric measure, with treatment phase as the independent variable. When the analysis of variance was significant, differences were analyzed with the Bonferroni t test to take into account multiple t tests. As the patients did not always complete the rating forms, the degrees of freedom differ slightly across the reported comparisons.

## RESULTS

### *Mood Changes*

The TSH levels and rating scale scores are shown in table 1. During $T_4$ replacement, four patients each had a score on the Beck Depression Inventory of at least 14, which is the cutoff score for indicating a moderate level of depression (21). Three patients had a score of at least 14 when receiving $T_3$, and five patients had a score of at least 14 when receiving no thyroid hormone replacement; three patients had a score of at least 14 during all three treatment phases. There was a significant effect of treatment phase on mood as measured by the Beck Depression Inventory (table 2). The patients' mean Beck score was significantly higher after the thyroid medication was discontinued than when they were taking either $T_4$ ($t=3.97$, $df=36$, $p<0.01$) or $T_3$ ($t=4.53$, $df=36$, $p<0.01$); no significant difference was noted between $T_4$ and $T_3$ ($t=0.55$, $df=36$, $p>0.05$). The ANOVA revealed a similar significant result (table 2) for treatment phase effect on the visual analogue scale self-ratings for mood ("most sad ever" to "most happy ever"). The mean self-rating scores during the three phases of treatment revealed no significant difference between $T_4$ and $T_3$ ($t=0.33$, $df=40$, $p>0.05$), but a significant change was observed between each medication and no medication ($T_4$ versus no medication: $t=3.04$, $df=40$, $p<0.05$; $T_3$ versus no medication: $t=2.71$, $df=40$, $p<0.05$). The lowest (more symptomatic) mean score on the visual analogue self-ratings for mood occurred after medication withdrawal (table 2).

An effect of treatment phase was also seen for anxiety, as measured with the visual analogue scale for anxiety ("most anxious ever" to "least anxious ever") (table 2). The mean self-rating scores during the three phases of the treatment revealed no significant change between $T_4$ and $T_3$ ($t=0.42$, $df=40$, $p>0.05$), but a significant difference was noted between each medication and no medication ($T_4$ versus no medication: $t=2.92$, $df=40$, $p<0.05$; $T_3$ versus no medication:

**TABLE 1. Characteristics and Responses to Thyroid Hormone Supplementation of 25 Thyroidectomized Patients**

| | | | | | TSH Level (μIU/ml)$^{a}$ | | | Beck Depression Score | | | Visual Analogue Scale Mood Rating$^{b}$ | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Patient | Sex | Age (years) | Months Since Thyroidectomy | $T_4$ Dose (μg/day) | With $T_4$ | With $T_3$ | No Medication | $T_4$ | $T_3$ | No Medication | $T_4$ | $T_3$ | No Medication |
| Psychiatric history | | | | | | | | | | | | | |
| Depression | | | | | | | | | | | | | |
| 1 | F | 42 | 16 | 175 | — | 28.8 | 130.8 | — | 11 | 11 | — | 47.5 | 28.4 |
| 2 | F | 53 | 78 | 200 | <0.1 | — | 20.9 | 14 | 15 | 31 | 75.9 | 74.3 | 12.3 |
| 3 | F | 55 | 17 | 150 | 2.0 | 2.8 | 49.0 | 2 | 0 | 9 | 53.7 | 53.7 | 51.6 |
| 4 | M | 38 | 139 | 100 | 10.8 | — | 135.9 | 14 | 2 | 12 | 59.8 | 65.5 | 65.2 |
| 5 | F | 55 | 52 | 100/150$^{c}$ | — | — | 4.4 | 28 | 23 | 33 | 53.0 | 68.6 | 54.5 |
| 6 | F | 40 | 256 | 300 | 2.6 | — | 240.0 | 6 | 3 | 7 | 69.3 | 48.6 | 34.9 |
| Other$^{d}$ | | | | | | | | | | | | | |
| 7 | F | 38 | 45 | 300 | <0.1 | <0.1 | 26.8 | 14 | 14 | 19 | 47.1 | 44.6 | 44.4 |
| 8 | F | 42 | 160 | 150 | 3.8 | 48.0 | — | 4 | 8 | — | 46.6 | 44.9 | — |
| 9 | F | 30 | 8 | 125 | <0.1 | 0.3 | 129.2 | 5 | 3 | 11 | 35.6 | 59.1 | 46.5 |
| 10 | M | 61 | 81 | 200 | — | 3.6 | 46.2 | 2 | 4 | 9 | 88.8 | 86.4 | 64.9 |
| No psychiatric history | | | | | | | | | | | | | |
| 11 | M | 21 | 56 | 200 | 1.9 | 7.1 | 479.0 | 3 | 3 | 4 | — | — | — |
| 12 | F | 35 | 64 | 200 | <0.1 | 40.6 | 154.3 | 4 | 9 | 14 | 56.8 | 56.5 | 23.9 |
| 13 | F | 59 | 29 | 150 | 0.1 | <0.1 | 137.9 | 1 | 2 | 1 | 49.8 | 48.6 | 48.4 |
| 14 | F | 38 | 3 | 100 | 0.3 | <0.1 | 173.1 | 9 | 5 | 4 | 53.2 | 52.1 | 55.1 |
| 15 | F | 41 | 51 | 125 | <0.1 | <0.1 | 50.2 | 6 | 3 | — | — | — | — |
| 16 | M | 24 | 66 | 200 | 0.8 | 0.9 | 85.7 | 1 | 1 | 2 | 61.5 | 36.4 | 26.0 |
| 17 | M | 39 | 197 | 200 | <0.1 | <0.1 | 60.4 | 3 | 2 | — | 47.4 | 46.0 | 27.8 |
| 18 | F | 59 | 165 | 200 | <0.1 | <0.1 | 23.8 | 0 | 3 | 17 | 53.0 | 52.0 | 45.2 |
| 19 | F | 42 | 68 | 200 | — | <0.1 | 51.5 | 3 | 0 | 5 | 62.9 | 49.9 | 50.6 |
| 20 | M | 62 | 9 | 150/200$^{c}$ | <0.1 | <0.1 | 63.2 | 5 | 5 | 7 | 48.7 | 51.4 | 55.0 |
| 21 | F | 53 | 68 | 100/150$^{c}$ | 0.8 | 1.3 | 98.6 | 2 | 3 | 4 | 48.2 | 51.2 | 51.6 |
| 22 | F | 54 | 6 | 125/150$^{c}$ | <0.1 | <0.1 | 85.2 | 0 | — | 1 | 96.7 | 90.4 | 88.7 |
| 23 | F | 27 | 23 | 200 | <0.1 | <0.1 | 66.3 | 0 | 7 | 4 | 50.9 | 51.5 | 49.3 |
| 24 | F | 36 | 97 | 200 | — | — | 57.1 | 2 | 1 | 8 | 63.3 | 68.7 | 72.4 |
| 25 | F | 34 | 97 | 150 | — | — | 39.4 | 4 | 3 | — | 52.8 | 49.6 | 48.2 |

[a] Normal range is 0.5 to 4.6 μIU/ml.

[b] Range is 0 to 100; a lower score indicates more sadness.

[c] Given on alternate days.

[d] Patient 7, bipolar II disorder; patient 8, adjustment disorder, depressed mood; patient 9, dysthymia; patient 10, organic delusional syndrome.

**TABLE 2. Mood Scale Scores of 25 Thyroidectomized Patients With and Without Thyroid Hormone Replacement**

| | | | | | Visual Analogue Scales | | | |
|---|---|---|---|---|---|---|---|---|
| | Beck Depression Inventory$^{a,b}$ | | Spielberger Anxiety Scale$^{a}$ | | Mood$^{c,d}$ | | Anxiety$^{c,e}$ | |
| Thyroid Hormone Replacement | Mean | SD | Mean | SD | Mean | SD | Mean | SD |
| $T_4$ | 5.50 | 6.40 | 36.54 | 11.58 | 57.95 | 14.22 | 57.81 | 15.14 |
| $T_3$ | 5.42 | 5.53 | 38.56 | 10.96 | 56.41 | 13.40 | 55.74 | 13.40 |
| None | 10.14 | 8.78 | 35.95 | 11.81 | 47.48 | 17.36 | 48.40 | 16.94 |

[a] A higher score indicates worse symptoms.

[b] $F=12.14$, $df=2, 36$, $p<0.01$ (analysis of variance with repeated measures).

[c] A lower score indicates more sadness/anxiety.

[d] $F=5.57$, $df=2, 40$, $p<0.01$.

[e] $F=4.97$, $df=2, 40$, $p<0.05$.

$t=2.50$, $df=40$, $p<0.05$). The mean scores indicated more anxiety with no medication (table 2). No effect of treatment phase on Spielberger scale anxiety scores was seen.

When the effect of treatment condition on the SCL-90 score was examined, significant effects were observed for depression ($F=14.94$, $df=2, 40$, $p<0.01$), anger-hostility ($F=5.20$, $df=2, 40$, $p<0.01$), and somatization ($F=9.02$, $df=2, 40$, $p<0.01$). These effects reflect more symptoms after medication withdrawal. No significant change over the three treatment phases was noted for anxiety, phobic anxiety, and paranoid ideation.

To examine lability of mood, we compared the standard deviations of the visual analogue scale self-ratings for mood across the three treatment conditions and found no evidence of an effect of treatment on this variable ($F=0.60$, $df=2, 40$, $p>0.05$).

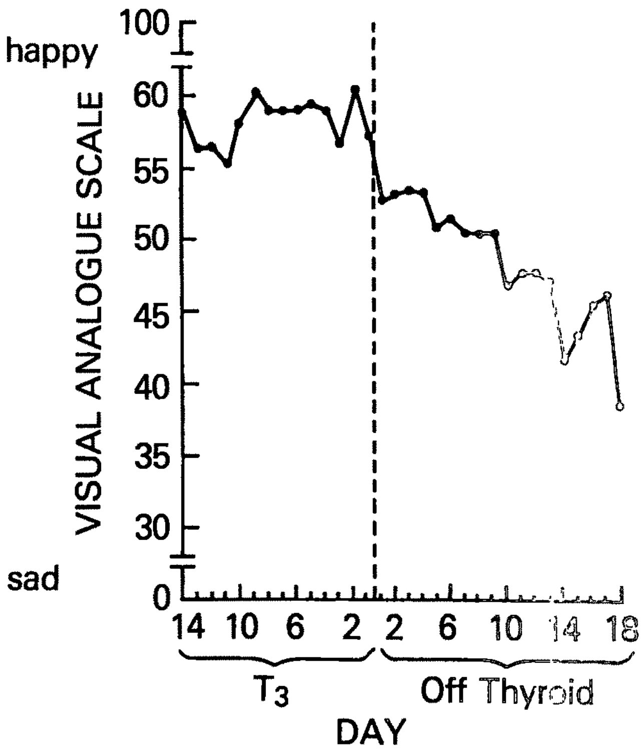
### *Cognitive Changes*

Comparison of the scores on the WAIS digit-symbol subtest during the three treatment phases revealed a significant effect ($F=7.32$, $df=2, 32$, $p<0.01$). This appeared to reflect a significant difference between $T_3$ and no medication ($t=3.74$, $df=32$, $p<0.01$); the patients performed better while receiving $T_3$. No significant change was noted in the patients' performance on the Cognitive Capacity Screening Examination between treatment phases. The visual analogue scale ratings for concentration ("unable to concentrate" to "thinking very clearly") indicated an effect of treatment phase on concentration ($F=10.62$, $df=2, 40$, $p<0.01$). No difference was observed between $T_4$ and $T_3$, but a significant difference was noted in mean concentration self-rating scores between each medication and no medication ($T_4$ versus no medication: $t=4.26$, $df=40$, $p<0.01$; $T_3$ versus no medication: $t=3.65$, $df=40$, $p<0.01$). These changes reflected poorer concentration without medication.

### *Other Visual Analogue Scale Ratings*

The pattern of significant differences between thyroid hormone treatment and no medication and nonsignificant differences between $T_4$ and $T_3$ was also found in the mean visual analogue self-ratings for physical comfort, mental tranquility, and energy level and in the global rating ("feel worst ever" to "feel best ever").

**FIGURE 1. Mean Visual Analogue Scale Self-Ratings for Mood of 20 Thyroidectomized Patients During and After $T_3$ Treatment**



The gradual but progressive decline in the mean visual analogue self-ratings for mood (sad/happy) after the patients stopped taking thyroid medication is illustrated in figure 1. This pattern reflects a gradual increase in the number of patients who experienced increases in sad mood after medication withdrawal. Ten patients had significant declines in their visual analogue self-ratings for mood when they stopped taking thyroid hormone replacement. A significant decline was defined as fulfilling one or both of the following criteria: 1) significantly lower mood ratings during the second week without medication than during the last week of thyroid medication and the first week without medication (ANOVA with repeated measures and post hoc t test) or 2) visual analogue scale mood self-ratings in 3 of the last 4 days without treatment that were more than two standard deviations below the mean rating with medication. The mean visual analogue self-ratings of mood during the medication phases and during the last 7 days without medication for the 10 patients who showed declines in mood ratings were 57.5 and 32.5, respectively, whereas the ratings for the 10 patients showing no decline were 58.4 and 58.5. Six of the 10 patients who rated themselves as more symptomatic (sad) had personal psychiatric histories of affective illness, whereas only two of the 10 patients who did not rate themselves as more symptomatic had positive histories of affective illness (Fisher's exact test: $p=0.08$). Seven of the 10 patients who experienced significant declines in mood self-ratings had measures of lability (the standard deviation of their visual analogue mood ratings while receiving medication) that were within the nine highest values seen among the 20 patients studied. Furthermore, the mean lability value during treatment was significantly higher in the patients who experienced significant declines in visual analogue self-ratings for mood after medication withdrawal ($t=2.29$, $df=18$, $p<0.05$). Finally, lability was inversely correlated with both the mood score (higher lability, more sad) on the last 4 days without thyroid hormone replacement ($r=-0.51$, $df=18$, $p<0.05$) and the mean of the mood rating score during the second week after discontinuation of thyroid hormone replacement ($r=-0.50$, $df=18$, $p<0.05$). In general, patients who showed a significant increase in the visual analogue self-rating of depression after the discontinuation of medication also showed a significant increase in symptoms according to the six other self-rating measures.

### *Psychiatric History*

Symptoms over the course of this study were compared in the patients with and without histories of psychiatric disorder (ANOVA with repeated measures). We found no effect of history of psychiatric disorder on any of the visual analogue scale self-ratings or on scores on the cognitive measures. However, the patients with psychiatric histories did have higher scores (significant effect of diagnosis) on the Beck Depression

Inventory (F=7.41, df=1, 17, $p<0.05$) and the Spielberger State Anxiety Scale (F=22.44, df=1, 18, $p<0.01$). Additionally, a Time by Diagnosis interaction was observed on the Beck scale (F=3.32, df=2, 34, $p<0.05$); patients with psychiatric histories had a higher mean Beck depression score during each of the treatment phases and showed a greater increase in Beck score after medication withdrawal than patients without past psychiatric histories. The mean Beck Depression Inventory scores during the $T_4$, $T_3$, and no-treatment phases were 10.6, 8.0, and 16.4 for patients with past psychiatric histories and 2.7, 3.5, and 6.4 for those without past psychiatric histories. For the patients with past psychiatric histories, the no-treatment score was significantly higher than the score with either treatment ($T_4$ versus no medication: paired t=2.95, df=7, $p<0.05$; $T_3$ versus no medication: paired t=6.09, df=7, $p<0.01$), but there was no difference between phases for those without past psychiatric histories.

### *Thyroid Function Tests*

One of the 19 patients who were given thyroid function tests during $T_4$ treatment had an abnormally high TSH level (normal range=0.5–4.6 μIU/ml). High levels were also found in four of the 19 patients tested during the $T_3$ treatment phase and 23 of the 24 patients tested during the no-medication phase. When the effect of treatment condition was examined without the five patients who were hypothyroid (i.e., had elevated TSH levels) during treatment, the only changes observed were in the comparisons of the mood and anxiety visual analogue scores during the $T_3$ and no-medication phases; both differences changed from statistically significant to just missing statistical significance. The change in scores on the anxiety subscale of the SCL-90 remained nonsignificant, but a strong trend was evident ($p=0.053$). The degree of TSH elevation after treatment withdrawal was unrelated to past personal psychiatric history, mood lability, or a self-rating of more sadness on the visual analogue scale for mood.

## DISCUSSION

Mood changes occurred when the patients stopped receiving thyroid hormone replacement. Depressive changes were revealed by each of the mood rating forms used: Beck Depression Inventory, SCL-90, and the visual analogue scale. The fact that only five patients scored 14 or more on the Beck scale when receiving no thyroid hormone replacement, compared with four patients during the $T_4$ phase, indicates that the depressive mood changes generally did not reach severe levels. However, the mood changes were evident even though the patients had stopped receiving thyroid hormone replacement only 2 to 3 weeks earlier. The relationship between depression and thyroid function has been noted in studies that have evaluated depressive changes in patients who are hypothyroid (1–4) and in studies that have investigated thyroid function in patients seen for depression (5, 6). This study is unique in that depressive mood changes were prospectively evaluated in thyroidectomized patients who suddenly stopped receiving thyroid hormone replacement. Because the patients were not blind to medication status, one cannot rule out an effect of the patients' knowledge that they were no longer receiving thyroid hormone replacement. Nonetheless, the pervasive nature of the increased symptoms and the range of latencies between the end of treatment and initial or maximal symptom decline suggest that the mood and behavioral changes experienced during the hypothyroid state reflected primarily the altered endocrine status.

An increase in anxiety after discontinuation of medication was indicated by the mean visual analogue scale anxiety scores but not by the Spielberger State Anxiety Scale or the SCL-90 anxiety subscale scores, although the change in mean SCL-90 anxiety subscale score just missed significance when the five patients who were hypothyroid during the medication phase were excluded. The reason for this discrepancy is unclear but may be related to how often the rating scales were administered. The SCL-90 and the Spielberger scale were administered at only one time point during each treatment phase, while the visual analogue scale was completed daily. Thus, the SCL-90 and Spielberger scores were more likely to be affected by transient situational influences.

The scores on the Cognitive Capacity Screening Examination did not indicate that treatment phase had any significant effect on cognitive performance. The results on the WAIS digit-symbol subtest did reveal a significantly better performance with $T_3$ than with no medication, whereas the scores with $T_4$ were nonsignificantly better than after medication withdrawal. It is possible that a learning effect due to test repetition may have obscured better performance during treatment on both of these measures. Whybrow et al. (3) found impaired cognitive function in their sample of severely hypothyroid patients. They noted a subjective impairment of recent memory and difficulty with psychological tests demanding attention, abstraction, and memory. The fact that our study did not reveal profound cognitive changes may be due to a number of factors: cognitive changes may only be significant in a more chronic hypothyroid sample, the scope of the testing might not have been sufficiently wide, or a learning effect may have obscured a significant result.

The patients also noted less global well-being, more physical discomfort, less mental tranquility, and less energy when not receiving thyroid medication. About one-half of the patients who completed the visual analogue scales rated themselves as more symptomatic when not receiving medication, although the no-medication phase lasted only 2 to 3 weeks. The fact that half of the patients did not rate themselves as more symptomatic and the different patterns of decline among the patients who had decreases in their visual analogue scale ratings imply that the patients in this study had variable vulnerabilities to mood changes when not receiving thyroid hormone replacement. The potential significance of this variable vulnerability to the mood-disrupting effects of thyroid perturbations is suggested by the finding that the patients with personal histories of affective illness and those who demonstrated the most lability of mood while taking thyroid medication were the most likely to rate themselves as more depressed when not receiving medication. We observed only a trend for the patients who experienced affective symptoms during thyroid withdrawal to have more personal history of affective illness. However, while patients both with and without histories of psychiatric disorder experienced increases in Beck depression scores (relative to scores with treatment), the increase was significant only in those with past histories of psychiatric (particularly affective) disorder.

While this study revealed a dramatic change in mood when the patients were not receiving medication, our results are not consistent with the hypothesis that the administration of $T_3$ and $T_4$ would have opposite effects on cerebral thyroid function in euthymic patients. However, these data do not permit comment on differences in the effects of $T_3$ and $T_4$ on patients with affective illness or as potentiators of the effects of antidepressants.

Finally, a variety of hypotheses have been proposed to explain the relationship between thyroid function and affective symptoms. In general, the potential mechanisms described have focused on interactions between thyroid hormone and catecholamines. In their review, Bilezikian and Loeb (22) cited several studies that indicated an increase in β-adrenergic receptors in the rat heart after exposure to thyroid hormone, with accompanying increases in adenylate cyclase activity. Further, the hyperthyroid state is associated with increases and the hypothyroid state is associated with decreases of β-receptor-mediated responses to catecholamines in the rat heart (22). On the basis of these data, an interaction between thyroid hormone and catecholamine receptors has been hypothesized as underlying the therapeutic effects of thyroid hormone augmentation of response to antidepressants. Given the postulated importance of catecholamine and β-adrenergic activity in affective disorders and their treatment, further study may identify historical or biochemical characteristics that increase susceptibility to the mood-altering effects of thyroid hormone dysregulation. This speculation derives at least partial support from our observation that patients who experienced increased affective symptoms (according to the Beck Depression Inventory) after thyroid hormone discontinuation were more likely to have personal histories of affective illness or of increased mood lability.

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# Transfers of Hospitalized Psychiatric Patients Under Medicare's Prospective Payment System

Marc P. Freiman, Ph.D., and Lloyd I. Sederer, M.D.

*Medicare's reimbursement policy provides payment incentives for hospitals to transfer psychiatric patients to another acute-care facility, especially when the destination facility is exempt from Medicare's prospective payment system. The authors found, however, that transfers were relatively infrequent in 1985, accounting for only approximately 3.4% of all psychiatric hospitalizations under Medicare. The most common type of transfer was from a nonspecialized general hospital bed to a Medicare-exempt psychiatric unit within the same hospital. Given that increasing financial pressures may result in a rise in the number of transfers, the authors discuss potential reforms of Medicare reimbursement for these cases.*

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There is a variety of hospital settings for the treatment of psychiatric illness. Under Medicare's prospective payment system, these settings are not all reimbursed in the same manner. Treatment in nonspecialized general hospital sites (scatter beds) is reimbursed according to diagnosis-related groups (DRGs), but treatment in approved psychiatric units in general hospitals, as well as treatment in psychiatric hospitals, is exempt from the DRG-based prospective payment system. Treatment in these facilities is reimbursed on the basis of its adjusted historical cost.

Differences in reimbursement methods may affect not only how treatment is provided within facilities but also where it is provided among the different types of facilities. The current prospective payment system policy, which provides incentives for exploiting the reimbursement system through transfer activity, may especially influence how and where treatment occurs.

When the prospective payment system was introduced, the Health Care Financing Administration indicated that eventually they expected to make a single payment to the final discharging hospital "that would arrange to provide compensation to the transferring hospital for a portion of the inpatient service" (1).

Current transfer policy distinguishes between transfers among facilities that are covered by the prospective payment system and transfers from a covered facility to an exempt one. Of crucial importance here is the fact that, for the purpose of prospective payment system reimbursement, an exempt psychiatric unit in a general hospital is considered a separate facility from the other wards of a hospital. Therefore, if a patient is moved from a general medical ward to an exempt unit within the hospital, this is considered a transfer.

For transfers between two hospitals covered by the prospective payment system, the source hospital receives a per diem payment, whereas the destination hospital receives a full DRG payment for the relevant diagnosis. (The total per diem payment for the transferring hospital cannot exceed the full DRG rate.) For transfers from a facility covered by the prospective payment system to an exempt one, the source facility receives a full DRG payment, but the receiving facility is paid on the basis of costs, as constrained by the Tax Equity and Fiscal Responsibility Act of 1982. This approach is based on the implicit assumption that a substantially different course of treatment is provided by specialized exempt facilities (2).

As noted, exempt facilities include public psychiatric hospitals, private psychiatric hospitals, and psychiatric units in general hospitals that specifically applied for and were granted exemptions. Nonexempt facilities include general hospitals with only scatter beds for the treatment of psychiatric illness, hospitals with nonexempt units, and scatter bed sites in general hospitals that have exempt units.

Given the variety of types of facilities for the treatment of alcoholism, drug abuse, and mental illness, some of which are exempt and some nonexempt, and the transfer payment mechanism already described, incentives currently exist for hospitals to exploit the prospective payment reimbursement system. A hospital may transfer patients from a nonexempt to an exempt facility at an early stage in treatment in order to receive full DRG payment while incurring only a portion of the costs. The transfer to the exempt site may or may not be medically indicated. If the patient is severely ill, the transfer itself may be appropriate, but the patient

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may be intentionally "dumped" by the transferring facility in order to avoid a financial loss in the provision of appropriate care. A general hospital may even exploit the system by transferring a patient from a scatter bed to its own exempt unit.

In this paper we seek to answer the following questions:

1. What is the magnitude of transfer activity for psychiatric patients under the prospective payment system?
2. What types of transfers are occurring? They may be from general hospitals to public psychiatric hospitals (where long-term custodial care can be provided). However, many other types of transfers are possible, including transfers within a single general hospital.
3. To what degree do the characteristics of transfers fit the assumption of prospective payment system policy, particularly for transfers from a nonexempt to an exempt facility? Are these transfer patterns consonant with appropriate medical practice, or do they reveal decisions that have been strongly influenced by reimbursement considerations?

In seeking answers to these questions, we analyzed transfer activity among the Medicare population with alcoholism, drug abuse, or mental illness during 1985.

## METHOD

The primary source of data for this analysis is the 1985 Medicare PATBILL file (3). This file contains records for every hospital discharge covered by Medicare Part A. We extracted from this file the population of all patients discharged from specialized psychiatric and substance abuse facilities (both units and hospitals), plus all patients with alcoholism, drug abuse, or mental illness discharged from short-term general hospitals and all remaining types of facilities (i.e., rehabilitation hospitals, children's hospitals, etc.). Each record contains data on patient characteristics, length of and charges for the hospital stay, and a hospital identifier that allows the identification of individual facilities.

Hospital charges are generally not reliable indicators of resource intensity among different hospitals because each hospital may use a different "markup" above costs to determine charges. Therefore, we calculated "Medicare reasonable costs" for each discharge. In constructing these costs we used per diem cost figures for routine and special care days and cost-to-charge ratios for ancillary services for each hospital, calculated from Medicare cost reports. All costs were adjusted to fiscal-year 1985 dollars and exclude capital and direct medical education costs. These latter costs are also excluded from DRG-based payment under the prospective payment system. A more detailed presentation of the data cleaning and file construction process is presented elsewhere (4).

A transfer was defined as having occurred when, for a Medicare beneficiary, the date of discharge for one facility stay was the same as the date of admission for another facility stay. PATBILL records allow us even to recognize transfers between scatter beds and an exempt unit within the same hospital because these are considered different facilities from the perspective of Medicare reimbursement.

For the purposes of this study we have divided psychiatric hospitals according to public or private ownership because of their generally different patient populations. General hospitals were divided into three categories: 1) general hospitals with an exempt psychiatric unit, 2) general hospitals with a nonexempt psychiatric unit, and 3) general hospitals with scatter beds only. Each hospital was assigned a category based on the most recent data available, either the 1985 Provider of Service file or the *1984 AHA Survey of Hospitals* (5).

The substance abuse DRGs have been reorganized since 1985, but sufficient diagnostic data are not available on the 1985 PATBILL discharge file to allow the use of these new DRGs. Consequently, we present data for all substance abuse DRGs combined.

General hospitals in states with prospective payment system waivers had little incentive to seek exemptions for psychiatric units because all hospital discharges were exempt from Medicare's prospective payment system. As a result, the coding on the PATBILL file for these states is generally insufficient to allow us to ascertain a transfer to an exempt unit within a general hospital. Therefore, the results presented here are for the 46 states, plus the District of Columbia, that did not have prospective payment system waivers.

Because the results presented here are based on data for the entire population of Medicare transfers of patients with alcoholism, drug abuse, or mental illness in the nonwaivered states in 1985, comparisons are presented without the use of statistical tests based on sampling theory.

## RESULTS

Approximately 3.4% of all discharges of patients with alcoholism, drug abuse, or mental illness (that is, approximately 10,000 out of 293,000) in 1985 in the nonwaivered states involved transfers. More than half of these transfers occurred among general hospital sites. More specifically, almost 30% of all transfers were within the same general hospital: 24.0% were from nonexempt scatter beds to an exempt psychiatric unit and 5.0% were from an exempt unit to a nonexempt unit. Almost 40% of all transfers were from scatter beds to exempt units within the general hospital sector: the transfers within hospitals (24.0%) and the transfers from nonexempt scatter beds in one hospital to exempt units of different hospitals (14.2%). Another 9% of all transfers were from one nonexempt general hospital site to another. These transfers could possibly be from a scatter bed in one general hospital

**TABLE 1. Characteristics of Frequent Types of Hospital Psychiatric Patient Transfers in States Without Prospective Payment System Waivers, 1985**[a]

| | Mean Length of Stay (days)[c] | | | Mean Cost (dollars) | | |
|---|---|---|---|---|---|---|
| Type of Transfer[b] | Source | Destination | Total[d] | Source | Destination | Total |
| From nonexempt to exempt in same general hospital | | | | | | |
| Transfers | 5.3 | 16.7 | 22.5 | 1,582 | 3,781 | 5,478 |
| All discharges[e] | 9.2 | 16.7 | 25.9 | 2,535 | 4,001 | 6,536 |
| From general hospital nonexempt to different general hospital exempt | | | | | | |
| Transfers | 6.3 | 18.8 | 25.6 | 1,722 | 4,314 | 6,115 |
| All discharges[e] | 9.3 | 16.7 | 26.0 | 2,356 | 4,001 | 6,357 |
| From general hospital nonexempt to private psychiatric hospital | | | | | | |
| Transfers | 6.0 | 22.3 | 28.7 | 1,566 | 5,609 | 7,259 |
| All discharges[e] | 9.3 | 21.1 | 30.4 | 2,356 | 5,094 | 7,450 |
| From general hospital nonexempt to different general hospital nonexempt | | | | | | |
| Transfers | 5.6 | 14.4 | 21.4 | 1,446 | 3,412 | 5,129 |
| All discharges[e] | 9.3 | 9.3 | 18.6 | 2,356 | 2,356 | 4,712 |
| From general hospital nonexempt to public psychiatric hospital | | | | | | |
| Transfers | 8.7 | 41.3 | 51.1 | 1,928 | 4,991 | 7,071 |
| All discharges[e] | 9.3 | 62.0 | 71.3 | 2,356 | 8,036 | 10,392 |
| From general hospital exempt to public psychiatric hospital | | | | | | |
| Transfers | 14.8 | 43.5 | 59.9 | 3,288 | 5,681 | 9,198 |
| All discharges[e] | 16.7 | 62.0 | 78.7 | 4,001 | 8,036 | 12,037 |
| From exempt to nonexempt in same general hospital | | | | | | |
| Transfers | 8.9 | 9.4 | 22.5 | 2,199 | 2,643 | 5,744 |
| All discharges[e] | 16.7 | 9.2 | 25.9 | 4,001 | 2,535 | 6,536 |

[a] Data based on Medicare Part A claims data and Medicare cost reports; 46 states plus the District of Columbia were nonwaivered.
[b] Exempt and nonexempt refer to units or beds that were exempt or nonexempt from Medicare's prospective payment system.
[c] Total number of days, which for a few transfers was greater than the number of Medicare-covered days.
[d] Data include a small proportion of multiple transfers during one hospitalization.
[e] Means for all discharges, not just transfers, for type of facility.

to a nonexempt psychiatric unit in another general hospital, but we cannot discern this from our data.

A large segment of the remaining transfers were from general to psychiatric hospitals: 9.4% were from nonexempt general hospital beds to private psychiatric hospitals, 7.5% were from nonexempt general hospital beds to public psychiatric hospitals, and 7.0% were from exempt general hospital units to public psychiatric hospitals. These three categories accounted for almost one-quarter of all transfers.

Table 1 presents data on lengths of stay for the most frequent types of transfers compared with those for all discharges of patients with alcoholism, drug abuse, or mental illness from these types of facilities. For example, for transfers from nonexempt scatter beds to an exempt unit within the same hospital, the average length of stay was 5.3 days for the scatter bed portion, substantially less than the 9.2-day average length of stay for patients with alcoholism, drug abuse, or mental illness treated in scatter beds without any transfer.

For all of the transfer types shown where the source was a nonexempt site in a general hospital, the average length of stay was clearly less than that for all discharges of patients with alcoholism, drug abuse, or mental illness from such locations. However, the average length of stay for the more specialized transfer destination was generally the same as or longer than that for the average discharge from these facilities (except when the destination was a public psychiatric hospital, where the length of stay after the transfer was about 3 weeks shorter than average).

For transfers from an exempt unit to a scatter bed within the same hospital, the length of stay in the exempt unit was much shorter than average (8.9 days versus 16.7 days) and was more likely to involve yet another transfer. These two findings suggest the development or discovery of a severe medical condition in the exempt unit that was better treated on a general medical ward of that hospital.

Finally, table 1 presents mean cost-per-case data for both the transfer sources and destinations. The results are similar to those for lengths of stay, as would be expected.

### *Hospital- and State-Level Results*

Although transfers were rather infrequent, it is important to determine whether they were isolated in a

**TABLE 2. Number of Psychiatric Patient Transfers Per General Hospital in States Without Prospective Payment System Waivers, 1985[a]**

| | Mean Number of Transfers | | | | | |
|---|---|---|---|---|---|---|
| | | Hospital Percentile | | | | |
| General Hospitals | N | 5th | 25th | Median | 75th | 95th |
| With exempt units (N=746) | | | | | | |
| Transfer source | 2.7 | 0 | 1 | 2 | 3 | 8 |
| Transfer destination | 3.2 | 0 | 1 | 2 | 5 | 10 |
| Internal transfer | 3.9 | 0 | 1 | 3 | 5 | 13 |
| With nonexempt units (N=354) | | | | | | |
| Transfer source | 2.4 | 0 | 0 | 2 | 3 | 8 |
| Transfer destination | 1.9 | 0 | 0 | 1 | 3 | 7 |
| Internal transfer | —[b] | | | | | |
| With scatter beds only (N=4,009) | | | | | | |
| Transfer source | 0.7 | 0 | 0 | 0 | 1 | 3 |
| Transfer destination | 0.1 | 0 | 0 | 0 | 0 | 1 |
| Internal transfer | —[b] | | | | | |
| Total (N=5,109) | | | | | | |
| Transfer source | 1.1 | 0 | 0 | 0 | 1 | 5 |
| Transfer destination | 0.7 | 0 | 0 | 0 | 0 | 4 |
| Internal transfer | —[b] | | | | | |

[a] Data based on 1985 Medicare Part A claims data; 46 states plus the District of Columbia were nonwaivered. Exempt and nonexempt refer to units or beds that were exempt or nonexempt from Medicare's prospective payment system.

[b] Not applicable.

few hospitals or occurred infrequently in many hospitals. If the former was the case, it may indicate that selected hospitals were aggressively using transfers as a means of exploiting prospective payment system reimbursement. If the latter was the case, clinical considerations would appear to have been a more likely motivation, although financial factors might still have influenced hospital behavior for a small number of cases.

Table 2 presents data on the number of transfers for general hospitals by type of hospital and by type of transfer. For general hospitals with exempt units, three sets of figures are presented: those where the hospital was the source of an outside transfer, those where the hospital was the destination of an outside transfer, and those where the transfer was within the hospital (that is, a transfer from a scatter bed to an exempt psychiatric unit).

For general hospitals with exempt units, each hospital was the source, on average, of almost three patients who were transferred to other hospitals. The distribution about this value was fairly narrow: only one in 20 hospitals with exempt units sent as many as eight patients a year to other hospitals. The numbers were nearly identical on the receiving end for these hospitals. Almost no hospital with exempt units received a large number of outside transfers. By contrast, general hospitals with exempt units had an average of nearly four internal transfers per hospital.

For hospitals with nonexempt psychiatric units, the average value and distribution where the hospital was a transfer source were very close to those for hospitals with exempt units. However, the average value for transfers where this type of hospital was the destination was substantially lower (see table 2).

Finally, hospitals with only scatter beds averaged less than one transfer per year, and only one in 20 transferred as many as three patients out. However, most general hospitals do not treat large numbers of Medicare patients with alcoholism, drug abuse, or mental illness.

We also analyzed transfer activity as a percentage of all Medicare psychiatric patients treated by a hospital. More than half of all general hospitals did not transfer a single psychiatric patient. Only about one out of 20 hospitals transferred 20% or more of their patients, and these were predominantly hospitals with a small number of psychiatric patients. For hospitals with exempt units, the median value for transfers from scatter beds to their own unit was 1.7%, and only one out of 20 hospitals transferred more than 6% of all their psychiatric cases in this manner. (Detailed tables are available from M.P.F.)

For public psychiatric hospitals, 9% of the average hospital's caseload resulted from transfers into the facility. This rate reflects the fact that these facilities frequently receive patients who have been deemed treatment failures at other types of facilities or whose clinical care is believed to be better rendered in the public sector. On average, 5.2% of the caseloads of private psychiatric hospitals represented transfers into the facility.

In general, these data indicate that transfers occurred infrequently even at the level of the individual hospital.

We also examined the rate of transfer activity at the state level. Transfers out of scatter beds in general hospitals may be easier in states with large public psychiatric hospital sectors (even though the results reported in the preceding section indicate that transfers to this sector account for only 15 of every 100 transfers). The distribution of transfer rates among states was fairly narrow, generally approximating the U.S. average of 3.4%. We compared these state-level rates with the number of public psychiatric beds per capita in each state and found little correlation between the availability of this type of bed and rates of transfer activity. It may be the case that the availability of beds by type of facility (e.g., general hospitals or public psychiatric hospitals) may be more important in determining the site of the initial admission than it is in determining the magnitude and direction of transfer activity.

### *DRG and Diagnostic Composition of Transfers*

We analyzed the DRG composition of transfers from a scatter bed to an exempt unit of the same general hospital, the most frequent type of transfer. Forty-three percent of the patients in scatter beds were diagnosed in DRG 430 (psychoses) before transfer. Another 20% of the transfers were diagnosed as falling into one of the substance abuse DRGs, an additional 14% were in DRG 426 (depressive neuroses), 13% were in DRG 429 (organic disturbance and mental retardation), and 6% were in DRG 425 (acute adjustment reaction).

We also examined the specific diagnoses (*ICD-9-CM*) for these patients. Almost 40% were diagnosed with some type of depressive disorder before transfer from a scatter bed. The most common diagnosis, representing 14% of all such transfers, was major depressive disorder, single episode (code 296.20).

When these same patients were transferred to exempt units within the same hospital, some changes in diagnosis occurred. Most notably, the number in DRG 430 increased by almost 10 percentage points. There were corresponding declines of more than four percentage points each for DRG 426 and for the substance abuse DRGs and a slightly smaller decline of more than three percentage points for DRG 425. The resulting DRG distribution for these transferred patients was similar to that for patients in exempt units who had not been transferred.

These diagnostic shifts for transferred patients most likely represent a refinement of the diagnoses. However, they might also be related to justifying, either for internal or peer review organization review, a transfer to an exempt unit that was motivated in part by financial considerations.

The second most frequent type of transfer was transfer from a scatter bed in one general hospital to an exempt unit in another general hospital. Both the DRG distributions and their changes were quite similar to those for transfers from a scatter bed to an exempt unit within the same hospital.

## DISCUSSION

The prospective payment system reimbursement policy considers a transfer to have occurred when a patient is "discharged" directly from one acute-care "facility" to another. By this definition, facility does not simply mean a hospital. A psychiatric unit that is exempt from Medicare's prospective payment system is considered a separate facility from the rest of the general hospital. Therefore, moving a patient from the medical ward to an exempt psychiatric unit within the same hospital is considered a transfer.

Current Medicare reimbursement policy creates a potential for hospitals to transfer patients from scatter beds to their own exempt units in an attempt to improve their collections. Hospitals also have an incentive to dump as soon as possible more severely ill patients to other hospitals, particularly exempt ones, because they will still receive a full DRG payment.

We found that transfers of Medicare psychiatric patients were relatively infrequent in 1985, accounting for only about 3.4% of all discharges. Almost all transfers originated in a general hospital and had an exempt site as the destination. The most common type was from a scatter bed to an exempt unit within the same hospital.

We also found that for the vast majority of hospitals, transfers amounted to only a small percentage of their psychiatric caseload. Consequently, we conclude that hospitals do not appear to be taking advantage of current transfer reimbursement policy by transferring patients to exempt units or dumping. Our finding that hospitals do not or cannot respond by all means available to increase revenues under the prospective payment system is not unique. For example, some analysts worried that the prospective payment system would encourage increased admissions of patients with less severe illness by hospitals attempting to profit from the fixed DRG payment rates. The decline in overall admissions that actually followed the introduction of prospective payment is evidence of the absence of this form of exploitation, prevented in part by the review systems put in place by Medicare (6).

The current prospective payment system regulations implicitly assume that a patient who is transferred from a nonexempt to an exempt facility receives two complete and separate courses of treatment. We find little support for this hypothesis for psychiatric transfers. However, for some of these transfers there may be justification for a brief initial stay in a scatter bed. Such stays may result from hospital admissions initiated by a general practitioner who cannot or chooses not to admit directly to a psychiatric unit. Patient denial or minimization may mask the true cause of the somatic symptoms, or the patient may resist anything other than a medical admission (7). This may be especially true for those with alcohol and/or drug problems, organic mental disorders of older age (dementias and organic affective disorders), and depressions. An initial scatter bed treatment site may also reflect a desire on the part of primary care physicians to manage their own patients. However, on evaluation and consultation during the scatter bed stay, transfer may be deemed appropriate. Other patients may need testing to rule out nonpsychiatric illness or medical care to stabilize the patient's condition that is more appropriately provided in a medical ward (e.g., in cases of substance abuse).

These factors would explain a combined length of stay that is substantially longer than the average length of stay for treatment in a specialized psychiatric facility alone. However, an alternative hypothesis is that inefficient care is being provided when a transfer of this type is involved. The short stay in a nonexempt bed may be the result of a fully occupied exempt unit and the patient's being held in a scatter bed until space becomes available in the unit. It may also result from poor diagnostic work on the part of the primary care physician in recognizing psychiatric illness (8). Finally, some transfers may also be motivated by an attempt to exploit the reimbursement system or to dump patients who are likely to be costly for a hospital to treat (relative to the DRG-based payment).

Although the 1985 data analyzed here do not provide strong indications that Medicare's transfer policy is being abused, the potential for abuse remains important, given the steady pressure on medical and surgical wards to decrease lengths of stay for Medicare patients. This is particularly true for exploitation by transferring patients from scatter beds to an exempt unit because this type of transfer can occur within an individual hospital. A transfer of a Medicare patient to any exempt site amounts to an early discharge, or shortened length of stay. From this perspective, moderately large exempt psychiatric units specializing in geriatric care become a great financial resource. We do not have data for this specific type of unit, but there has been a general growth in the number of beds in specialized psychiatric facilities in recent years (9).

This potential and the absence of justification for scatter bed stays of more than a few days both indicate that the prospective payment system reimbursement policy for transfers should be revised. It appears more appropriate to pay on a per diem basis for the first part of a transfer for psychiatric patients, regardless of whether the destination is exempt or nonexempt. That is, the source facility would receive a payment based on the number of days and the destination facility would get either a DRG payment or costs constrained by the Tax Equity and Fiscal Responsibility Act of 1982, depending on whether the facility was covered or exempt from the DRG system. This approach would decrease the financial incentives for transferring patients but still provide payment for the initial portion or a transfer. It would also be compatible with a per diem utilization review procedure, which may be a useful adjunct with regard to treatment for mental illness in a scatter bed site (10).

Making a single prospective payment for an entire hospital stay, regardless of whether a patient is transferred, represents a conceptual ideal for a prospective payment system for individual hospital admissions. However, as we noted in the beginning of this paper, the Health Care Financing Administration does not yet view such an approach as feasible.

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# Short REM Latency in Primary Alcoholic Patients With Secondary Depression

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*Primary alcoholic patients with secondary depression had significantly shorter REM latency and less non-REM sleep than alcoholics without other psychiatric diagnoses and normal control subjects. Both patient groups had significantly longer sleep latency and less sleep efficiency, total sleep time, and delta sleep than control subjects.*

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Objectively measured sleep disturbances are common in patients with depression (1–3) and in newly abstinent alcoholic patients (4–6). Both groups of patients show prolonged sleep latency; less total sleep time, non-REM sleep, and delta (stages 3 and 4) sleep than normal subjects; and poor sleep efficiency (percentage of time in bed that is actually spent asleep). In addition, depressed patients show short REM latency (time from sleep onset to the first REM period), elevated REM density (a measure of ocular activity during REM sleep), and increased duration of the first REM period (1–3).

Many patients with primary alcoholism meet formal diagnostic criteria for secondary depression while drinking or during the first weeks of withdrawal (7, 8). Except for one abstract (9), there has been only one previous report of a study that specifically examined the polygraphically recorded sleep of primary alcoholic patients with secondary depression. Using the Research Diagnostic Criteria, Giles et al. (10) found no significant difference in REM latency between 26 patients with primary alcoholism and secondary depression (who had apparently been abstinent for several years) and 19 patients with primary disorders other than substance abuse who had secondary depression.

In the present study we compared polygraphic sleep recordings of patients with primary alcoholism without depression, patients with primary alcoholism and secondary depression occurring during the first 2 weeks of withdrawal, and normal control subjects. Because of the large number of sleep variables normally measured in our laboratory and the relatively small number of subjects, we focused on five sleep measures. We predicted that both groups of patients would show prolonged sleep latency and less total sleep time, non-REM sleep stages, and sleep efficiency than the control subjects; on the other hand, we predicted that the depressed alcoholic patients would have a shorter REM latency than the nondepressed alcoholic patients and the normal control subjects.

## METHOD

This study compared 31 normal control subjects, 12 alcoholic depressed patients, and 21 alcoholic nondepressed patients. All subjects were male. The control subjects were recruited from the community. The 33 patients were chosen from among 56 inpatients who were studied during the first week of hospitalization and who were participating in a longitudinal study of primary alcoholism. To create relatively "pure" matched groups of control subjects and depressed and nondepressed alcoholic patients, we excluded seven patients with definite or probable secondary drug abuse, two patients with secondary anxiety disorder,

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and 14 patients over the age of 52 for whom we did not have age-matched control subjects. All subjects underwent careful screening—including, in most cases, all-night finger oximetry and a tibial electromyogram (EMG) on the adaptation night to rule out sleep apnea and periodic leg movements—to exclude anyone who had another major medical disorder or had used psychoactive drugs within the past 2 weeks. The depressed and nondepressed alcoholic patients were diagnosed following a formal, structured diagnostic interview based on *DSM-III* criteria, as modified by Schuckit (7).

All-night polygraphic sleep records (EEG, electro-oculogram, EMG, and ECG) were obtained for 2 or 3 consecutive nights. Since control subjects, but not patients, showed a "first night effect," and a greater proportion of the control subjects than of the patients had a third night of polysomnography, only data from the second night are presented here.

For the sake of completeness, we present the data on 23 sleep measures on which analyses of variance were performed. We used the Newman-Keuls test to compare the three groups. Focusing on the five sleep measures of particular interest, we did Bonferroni corrections for an experimentwise alpha standard, requiring that instead of the usual $p<0.05$, the value for statistical significance be $p<0.01$. In keeping with a previous study (1), we selected three sleep measures—sleep latency, non-REM sleep, and REM latency corrected (REM latency minus intervening awake time)—as important domains of interest and conducted a linear discriminant function analysis of these measures.

## RESULTS

As shown in table 1, the three groups were matched for age. Both the depressed and the nondepressed alcoholic patients had histories of moderately severe alcohol consumption and did not differ from each other on any clinical or demographic variable, except that the depressed group tended to have higher scores on the Hamilton Rating Scale for Depression than the nondepressed group.

Both groups of patients had a moderate to severe disturbance of sleep compared with the age-matched control subjects. As predicted, differences on the five sleep measures of particular interest—total sleep time, sleep latency, sleep efficiency, non-REM sleep, and REM latency corrected—were statistically significant after application of the Bonferroni correction. Compared with the normal control subjects, both patient groups showed significantly longer sleep latency and less sleep efficiency and total sleep time. The loss of sleep was at the expense of non-REM sleep, especially delta (stages 3 and 4) sleep. The patients' REM sleep time was about the same as, but their percentage of REM sleep was significantly greater than, that of the control subjects.

The depressed alcoholic patients were significantly different from the control subjects on slightly more sleep measures than were the nondepressed alcoholic patients (13 measures versus 10). Unlike the nondepressed patients, they had a significantly later bedtime, a shorter total recording period, less stage 2 sleep, and shorter REM latency and REM latency corrected than the control subjects.

Compared with the nondepressed alcoholic patients, the depressed alcoholic patients had a significantly shorter REM latency and REM latency corrected, a significantly later sleep-onset time, and significantly less non-REM sleep. The nondepressed alcoholic patients had significantly more stage 1 sleep and a significantly higher percentage of stage 1 sleep than either the depressed alcoholic or the normal control subjects and significantly longer duration of the first REM period than the control subjects. The depressed alcoholic patients also tended to have a longer first REM period than the control subjects; this comparison just missed statistical significance.

The linear discriminant function analysis correctly classified 71.9% of the subjects: 29 (93.5%) of the 31 control subjects, five (41.7%) of the 12 depressed alcoholic patients, and 12 (57.1%) of the 21 nondepressed alcoholic patients. Two (6.5%) of the control subjects were misclassified as nondepressed alcoholic. Of the depressed alcoholic patients, two (16.7%) were misclassified as control subjects and five (41.7%) as alcoholic only. Of the nondepressed alcoholic patients, six (28.6%) were misclassified as control subjects and three (14.3%) as depressed alcoholic. In no case did use of the jackknife procedure produce less than 71% of correctly classified cases.

## DISCUSSION

These results are consistent with the concept that short REM latency is a biological state marker associated with formally diagnosed (i.e., by *DSM-III* criteria) depression, secondary as well as primary or endogenous (1–3). It should be noted that REM latency was not statistically correlated with scores on the Hamilton depression scale. Therefore, in studies of biological or clinical states, it is necessary to consider depression, for example, from a diagnostic as well as from a symptomatic viewpoint.

The two patient groups shared other sleep abnormalities, such as difficulty falling asleep, poor sleep efficiency, and loss of total sleep time, non-REM sleep, and delta sleep. These sleep disturbances are probably relatively nonspecific from a diagnostic point of view, since they were found in both groups and have been described in varying degrees in patients with other disorders, such as insomnia, schizophrenia, dementia, and central neurological problems (1). Interestingly, REM sleep time was preserved in this study. Neither group of patients showed elevated REM density, either for the whole night or for the first REM period, although this has been reported in some studies of depressed patients (1–3). Both patient groups showed

**TABLE 1. Clinical and Demographic Characteristics and All-Night Sleep Data for 31 Normal Control Subjects, 12 Primary Alcoholic Patients With Secondary Depression, and 21 Primary Alcoholic Patients Without Depression**

| | Control Subjects | | Depressed Alcoholic Patients | | Nondepressed Alcoholic Patients | | F | |
|---|---|---|---|---|---|---|---|---|
| Item | Mean | SD | Mean | SD | Mean | SD | (df=2, 63) | p |
| Age (years) | 39 | 7 | 38 | 7 | 41 | 7 | 1.0 | n.s. |
| Education (years) | — | — | 12 | 2 | 12 | 2 | 0.0 | n.s. |
| Duration of alcoholism (years) | — | — | 8 | 8 | 8 | 9 | 0.0 | n.s. |
| Age at onset of alcoholism (years) | — | — | 30 | 8 | 33 | 7 | 1.0 | n.s. |
| Days sober at time of sleep study | — | — | 14 | 7 | 17 | 6 | 1.5 | n.s. |
| Number of months out of the past 3 in which drinking occurred | — | — | 2.8 | 0.6 | 2.8 | 0.5 | 0.1 | n.s. |
| Days drinking per month | — | — | 25 | 7 | 22 | 9 | 0.7 | n.s. |
| Drinks per drinking day | — | — | 12 | 10 | 15 | 6 | 1.4 | n.s. |
| Maximum number of withdrawal symptoms | — | — | 6 | 4 | 6 | 4 | 0.0 | n.s. |
| Hamilton depression score | — | — | 15 | 6 | 11 | 7 | 3.7 | <0.06 |
| γ-Glutamyltransferase (mU/ml) | — | — | 79 | 92 | 51 | 43 | 1.9 | n.s. |
| Bedtime (clock time) | 23:33 | 47[a] | 00:20 | 14[b] | 23:44 | 51 | 3.3 | <0.05 |
| Sleep onset (clock time) | 23:42 | 48[a] | 00:47 | 8[b] | 00:06 | 48[c] | 6.7 | <0.003 |
| End of sleep (clock time) | 06:19 | 47[a] | 06:23 | 35 | 06:16 | 35 | 0.1 | n.s. |
| Total recording period (minutes) | 414 | 48 | 365 | 64[b] | 396 | 58 | 3.5 | <0.05 |
| Total sleep time (minutes) | 377 | 49 | 311 | 58[b] | 347 | 52[b] | 7.4 | <0.002[d] |
| Time awake in bed (minutes) | 17 | 24 | 15 | 15 | 16 | 14 | 0.1 | n.s. |
| Sleep latency (minutes) | 9 | 7 | 27 | 16[b] | 22 | 14[b] | 14.0 | <0.001[d] |
| Early morning awake (minutes) | 5 | 10 | 1 | 2 | 3 | 4 | 1.0 | n.s. |
| Sleep efficiency (%) | 91.3 | 5.9 | 85.6 | 6.7[b] | 87.8 | 4.5[b] | 5.1 | <0.009[d] |
| Non-REM sleep (minutes) | 282 | 42 | 215 | 45[b] | 248 | 40[b,c] | 12.1 | <0.001[d] |
| Stage 1 sleep | | | | | | | | |
| Minutes | 15 | 14 | 13 | 6 | 25 | 12[b,c] | 5.3 | 0.008 |
| % | 4.1 | 3.5 | 4.1 | 2.1 | 7.2 | 3.4[b,c] | 6.3 | 0.003 |
| Stage 2 sleep | | | | | | | | |
| Minutes | 231 | 52 | 190 | 38[b] | 207 | 37 | 4.0 | 0.022 |
| % | 60.9 | 10.7 | 61.1 | 7.0 | 59.8 | 8.2 | 0.1 | n.s. |
| Delta sleep | | | | | | | | |
| Minutes | 36 | 28 | 13 | 16[b] | 17 | 23[b] | 5.9 | 0.005 |
| % | 9.8 | 8.0 | 3.8 | 4.8[b] | 4.5 | 6.1[b] | 5.3 | 0.008 |
| REM sleep | | | | | | | | |
| Minutes | 95 | 24 | 97 | 26 | 99 | 27 | 0.2 | n.s. |
| % | 25.1 | 5.6 | 31.1 | 5.8[b] | 28.5 | 6.1[b] | 5.2 | 0.008 |
| REM latency (minutes) | 74 | 30 | 46 | 28[b] | 67 | 23[c] | 4.3 | 0.02 |
| REM latency corrected[d] (minutes) | 68 | 21 | 44 | 25[b] | 62 | 20[c] | 5.2 | <0.01[d] |
| REM density[e] | 1.8 | 0.6 | 2.0 | 0.7 | 2.1 | 0.8 | 0.9 | n.s. |
| Duration of first REM period (minutes) | 17 | 8 | 27 | 19 | 26 | 16[b] | 3.5 | 0.037 |
| REM density[f] during first REM period | 1.5 | 0.7 | 1.9 | 1.0 | 2.1 | 0.9 | 2.7 | n.s. |

[a] SD is in minutes.

[b] Significantly different from the normal control subjects (Newman-Keuls test, $p<0.05$).

[c] Significantly different from the depressed alcoholic patients (Newman-Keuls test, $p<0.05$).

[d] Differences on this measure of special interest were still statistically significant ($p<0.05$) after the Bonferroni correction.

[e] REM latency minus intervening awake time.

[f] Scored on a scale of 0 to 8 per minute of REM sleep.

greater duration of the first REM period, although it was statistically significant only for the nondepressed alcoholic patients.

Only one sleep measure appeared to reflect an additive effect related to the dual diagnosis (alcoholism/depression) compared with the single diagnosis (alcoholism). Non-REM sleep was less in both patient groups than in the normal control subjects, but it was significantly less in the depressed alcoholic patients than in the nondepressed alcoholic patients.

The depressed alcoholic patients had a significantly later sleep onset time than the nondepressed alcoholic patients. This probably contributed not only to the reduced non-REM time but to the shorter REM latency in the former group than in the latter. Interestingly, however, the nondepressed patients had significantly more stage 1 sleep and a higher percentage of stage 1 sleep than the depressed patients. Stage 1 is usually considered to be a transitional sleep state between wakefulness and "real" sleep. Increased amounts may reflect more shallow or lighter sleep.

The results of the linear discriminant function analysis suggest that even a limited sample of three sleep measures (sleep latency, non-REM sleep, and REM latency corrected) provided a reasonably successful separation of the three diagnostic groups (>71%), especially the separation of control subjects from patients (93.5%). It was least successful for the depressed alcoholic patients, equal numbers of whom it classified as depressed alcoholic and nondepressed alcoholic. As in our previous successful discriminant function classification of depressed, insomniac, and control subjects (1), it would be advantageous in future studies to compare larger numbers of subjects, which would permit entry of more sleep measures and the blind classification of new subjects.

These results are consistent with the possible importance of dual diagnosis in alcoholism. Schuckit (7, 8) has emphasized that patients with primary and secondary alcoholism have different prognoses. Longitudinal studies are underway to determine the natural history of both the clinical course and the sleep disturbance in primary alcoholic patients with and without secondary depression.

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# Pharmacotherapy of Four Men With Paruresis

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*Four men with paruresis received trials of atenolol or phenelzine or both. Atenolol was effective in one patient. Three patients had a poor response to phenelzine, and they all experienced troublesome side effects.*

(Am J Psychiatry 1990; 147:109–111)

Paruresis is a functional disorder of micturition involving the inability to urinate in the presence of others (1). Especially provocative are the lack of visual privacy, the presence of strangers, and the proximity of others (2), which produce feelings of anxiety, anger, body shyness, and increased autonomic arousal. Increased sympathetic outflow produces active contraction of the internal and external urethral sphincters, both of which must be relaxed for urination (3).

Individuals with paruresis (alternatively known as "bashful bladder syndrome" or "psychogenic urinary retention") would be diagnosed according to *DSM-III-R* as having a nongeneralized social phobia. Monoamine oxidase inhibitors and beta blockers, which have been found to be beneficial in social phobia (4, 5), could therefore be helpful for paruresis. Effective treatment for paruresis is important, since phobic avoidance of public restrooms and even friends' homes often develops, leading to severe functional impairment for the individual.

Following earlier reports of treatment with psychodynamic psychotherapies and hypnosis, behavioral

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management of paruresis has been suggested, including systematic desensitization, prolonged exposure, classical conditioning, assertiveness training, cognitive restructuring, and paradoxical intention (reviewed in reference 2). Combined approaches such as in vivo desensitization and paradoxical intention appear to be the most successful. However, such methods are not universally beneficial, and this has kindled interest in pharmacotherapy.

Accounts of pharmacotherapy for paruresis are limited. Furosemide was tried as an adjunct to exposure therapy with five patients who received 20–40 mg 1 hour before each session to ensure adequate urinary output (6). This led to six voidings per hour, which facilitated treatment, with significant improvement in all five patients. Phenoxybenzamine, 10 mg orally b.i.d., and diazepam, 2 mg orally b.i.d., had little effect in a paruretic man who had previously tried behavioral and psychodynamic psychotherapy, without success (7).

Paruresis resembles other discrete social phobias. One study found that patients with paruresis had significantly higher scores on performance anxiety than normal control subjects, which suggests a relationship between the two syndromes (8). Atenolol, a cardioselective β-adrenergic blocker, has been shown to be useful in reducing autonomic symptoms that accompany performance anxiety. It could also be beneficial in paruresis, where unwanted sympathetic arousal plays a crucial role in urinary retention. In a placebo-controlled comparison of atenolol and phenelzine for the treatment of 41 subjects with social phobia, atenolol seemed effective for patients with discrete social anxiety but not general social anxiety, whereas phenelzine was found to be superior overall to atenolol and placebo (5).

We report here on the pharmacotherapy of four men with paruresis who participated in our ongoing placebo-controlled comparison of phenelzine and atenolol for the treatment of social phobia (5).

## METHOD

After comprehensive clinical evaluation and informed consent, patients entered the study, which consisted of the following three phases: 1) 1 week of placebo, administered in a single-blind manner, then an 8-week double-blind, placebo-controlled phase with maximum attainable daily doses of 90 mg of phenelzine and 100 mg of atenolol, 2) an 8-week treatment continuation phase for responders, and 3) a placebo-controlled, double-blind discontinuation phase with 4 weeks of tapering and 4 weeks without medication (5).

## RESULTS

Data from patients 1 and 2, who received adequate trials, are detailed in the Case Reports section, and there are limited descriptions of patients 3 and 4, who terminated treatment prematurely. All four patients were rated as being moderately ill according to the Clinical Global Impression scale (CGI); their scores on the Hamilton Rating Scale for Anxiety ranged from 2 to 9. Their scores on the Hamilton Rating Scale for Depression ranged from 3 to 5, which reflects minimal depressive symptoms. On the 7-point Liebowitz Panic and Social Phobic Disorders—Severity Rating, all four patients had a rating of 4 (moderate) on overall severity. Patients 1, 3, and 4 were found to have marked phobic avoidance, and patient 2 had moderate avoidance; anticipatory anxiety was considered marked in patients 1 and 4 and moderate in patients 2 and 3. Clinically, patient 1 was able to lead a generally successful life with the exception of a circumscribed phobia. Patients 2–4 had severely restricted their lifestyles as a result of their paruresis.

Termination data for patients 1 and 2 were available at 20 weeks and 8 weeks, respectively. At the end of the study patient 1 was deemed to be minimally improved; his CGI rating reflected mild illness, his Hamilton depression score was 7, and his Hamilton anxiety score had dropped from 7 to 4. His Liebowitz scale score for overall severity had dropped by one point, to a rating of mild, and his avoidance and anticipatory anxiety were rated as moderate. On the other hand, all termination ratings (CGI, Hamilton anxiety and depression scales, and the Liebowitz scale) for patient 2 were unchanged from baseline, reflective of his lack of response.

## CASE REPORTS

*Case 1.* Mr. A, a 38-year-old divorced man, presented with a 30-year history of paruresis. He recalled first having had difficulty urinating in his father's presence. He was unable to use a public urinal if others were present or if others were waiting for him to return or to use the restroom. He avoided crowded facilities and limited his fluid intake when going out. He had overcome anxiety over public speaking through a public speaking course.

Mr. A showed some improvement by week 8 on a regimen of phenelzine, 45 mg/day in the double-blind phase, i.e., he was able to use the urinal in a busy restroom when he was alone. At week 18, during the discontinuation phase, Mr. A relapsed and the phenelzine dose was increased to 60 mg/day. The phenelzine caused urinary hesitancy, which increased his anxiety, and the dose was lowered to 45 mg/day. This side effect cleared, and he showed minimal improvement through the end of the study. Phenelzine was then tapered and atenolol was prescribed openly, to a maximum daily dose of 100 mg. After 8 weeks of atenolol treatment, Mr. A's anxiety and avoidance were markedly diminished. He was able to urinate in the presence of others, in crowded restrooms, and when others were waiting. Follow-up showed that 4 months later, he continued to do well on a regimen of atenolol and had made further gains through adjunctive behavior therapy.

*Case 2.* Mr. B, a 33-year-old married man, had a history of paruresis since age 12. He was unable to use any public restroom, even if it was empty, which kept him from attending school and traveling away from home. Prior weekly psychotherapy for several months had had no effect on his paruresis.

After 8 weeks on a regimen of atenolol, 100 mg/day administered in a double-blind manner, his anticipatory anxiety and avoidance were unchanged. Atenolol was tapered and an open trial of phenelzine was begun. Mr. B showed minimal improvement over 10 weeks with a maximum dose of 75 mg/day, but he was still unable to urinate in a public restroom. He also complained of urinary hesitancy and sexual side effects and discontinued the medication. His therapist tried single doses of bethanechol chloride at 25 mg/day and then at 37.5 mg/day, without benefit. Behavioral therapy was recommended but refused.

*Case 3.* Mr. C, a 40-year-old single man, had a 36-year history of being unable to urinate in public facilities and in recent years had developed almost complete phobic avoidance, working out of his home. He denied other social phobic symptoms. After 2 weeks on a regimen of phenelzine, up to 60 mg/day, Mr. C complained of a prolonged erection, and the medication was discontinued. Atenolol, 50 mg/day, was prescribed openly; after one dose, the patient reported a burning sensation upon micturition and refused further treatment.

*Case 4.* Mr. D, a 44-year-old divorced man, had a history of paruresis dating back to high school. His near complete avoidance of facilities outside his home limited his social life. Prior treatment included hypnotherapy, which had been unsuccessful, and a brief trial with imipramine, which had worsened his symptoms, although he denied urinary retention. After 2 weeks of atenolol, 50 mg/day administered in a double-blind fashion, Mr. D noticed no improvement and refused further treatment.

## DISCUSSION

Despite phenelzine's efficacy in social phobia, it does not appear to be helpful in paruretic patients. Cases 1 and 2 imply that the development of even mild urinary hesitancy leads to increased anxiety and phobic avoidance. Thus, phenelzine is not indicated in paruresis alone, and its side effects should be weighed carefully against benefits in patients who have generalized social phobia and paruresis.

Atenolol was successful in the first case but not in the second. The patient with the least phobic avoidance responded to atenolol, while the other three patients, all of whom had near total phobic avoidance, showed no improvement or terminated treatment prematurely. It is possible that patient 1 might have improved with behavioral therapy alone, since he had previously overcome anxiety over public speaking with a public speaking course and was currently able to further his gains with atenolol through adjunctive behavioral treatment.

In summary, these findings suggest that pharmacologic treatment is not an easy solution to paruresis. Atenolol may be useful for the symptoms of autonomic hyperarousal, in particular contraction of the urethral sphincters, which prevents urination. Further research is needed to determine whether atenolol offers any advantage over nonpharmacologic modalities (e.g., behavioral or psychodynamic psychotherapy) in patients with limited phobic avoidance. However, patients who have developed severe secondary avoidance most likely require a multimodal approach that combines medication and cognitive behavioral therapy or supportive psychotherapy.

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# Psychiatric Patients' Belief in General Health Factors and Sin as Causes of Illness

William Sheehan, M.D., and Jerome Kroll, M.D.

*Of 52 psychiatric inpatients, 81% believed that factors such as proper diet, sleep, and exercise affect the development of illnesses, and 23% believed that sin-related factors, such as sinful thoughts or acts, have such an effect.*

(Am J Psychiatry 1990; 147:112–113)

In a previous paper (1), we reported the results of a study investigating the religious beliefs, attitudes, and practices of a cohort of psychiatric inpatients. In the present study, we inquired into the extent to which religious and traditional lay notions of the etiology of disease influence psychiatric patients' beliefs about the causes of illness in general and of their own illnesses in particular.

## METHOD

The patient sample and study methods have been described previously (1); there were 19 men (37%) and 33 women (63%). Their diagnoses were major depression (N=16), manic episode (N=11), schizophrenia (N=10), personality disorder (N=10), and anxiety disorder (N=4); one patient in the sample was not diagnosed.

For the present study, we developed a 14-item checklist (available on request) consisting of eight items from the work of Rippere (2) that cover general beliefs about causes of illnesses and six new items relating to the role of sinful thoughts and behaviors in causing illnesses. We examined demographic characteristics and psychiatric diagnoses to determine their relationships to beliefs about factors affecting health and illness, using chi-square tests with Yates correction; total numbers of positive responses for general and sin-related factors were compared with t tests.

## RESULTS

Of the 52 patients in the study, 81% (N=42) expressed the belief that diet, exercise, sleep, the weather and climate, how one lives one's life, the type of person one is, and/or controlling one's emotions affect whether or not a person becomes ill. Two-thirds of the patients (67%, N=35) disagreed with the statement that keeping check on one's emotions is not much use in preventing illness, and only one-third (33%, N=17) agreed with the statement "I have no control over whether I become ill or not."

Belief in the role of sin in causing illnesses was endorsed by a considerably lower proportion. Of the 52 patients, 19% (N=10) said they believed that illnesses can occur as punishment for sinful thoughts, and 23% (N=12) thought illness could be the result of sinful acts. When the statement was phrased in more personal terms, 27% of the patients (N=14) said they believed that whether they sin or not has an influence on whether they become ill, and 10% (N=5) agreed that they were in the hospital because they had sinned. Nineteen percent of the patients (N=10) said they believed they would not get better if they did not do penance, and 42% (N=22) said they believed that living a moral life helps prevent illness.

Depressed patients endorsed an average of 0.9 sin-related items, compared to an average of 2.2 sin-related items for schizophrenic patients ($t=1.91$, $df=24$, $p=0.068$). A significantly higher percentage of the patients in the personality disorders group (mainly borderline and bulimic patients) (40%, N=4) than in the other diagnostic groups (2%, N=1) endorsed the specific item "I am in the hospital now because I have sinned" ($\chi^2=8.93$, $df=1$, $p=0.003$). No depressed patients and 10% of the schizophrenic patients (N=1) expressed agreement with this statement. Similarly, only 6% of the depressed patients (N=1) agreed that they would not get better if they did not do penance for their sins, compared with 40% for both the schizophrenic patients and the personality disorder patients (N=4).

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## DISCUSSION

One of the enduring questions about the significance of the recent religious revival in the United States is the extent to which religious beliefs permeate the attitudes and conduct of everyday life. In particular, we have been interested in whether lay people employ religious explanations in their understanding of the causes of mental illness. Our previous research results (3, 4) contradicted the common assumption about the Middle Ages that, since medieval Europe was a Christocentric culture, all explanatory systems were primarily religious and superstitious in nature.

In our present study, 81% of the psychiatric patients indicated belief in general health factors (e.g., exercise, proper diet, weather) and 23% endorsed sin-related factors (e.g., sinful thoughts or acts, living an amoral life) as causes of illnesses. The present study also supports the finding of previous studies (1, 5) that the role of guilt in depression appears to have been overestimated. One possible explanation for the low rate of endorsement of sin-related items by depressed patients might be effective education on the "biochemical imbalance" theory of depresssion (6), but we did not think to ask for such information. In any event, our findings suggest that depressed patients do not appear to be particularly preoccupied with issues involving sin and morality and do not believe, as much as several other groups of patients, that moral transgressions are responsible for the occurrence of illness.

The influence of our religious heritage on our beliefs about causes of illnesses appears to be ambiguous. Scientific principles and knowledge have not entirely superseded earlier notions of how illnesses develop or what measures could prevent or ameliorate illnesses. Superstitions, specific religious tenets, premodern medical theories, and modern scientific understandings all seem to exist concurrently in our culture, in different combinations, intensities, and emphases in different groups and geographic subcultures.

Since humans appear constitutionally designed to seek meanings for the events in their lives or to impose meaning on them, it is not surprising that they will often use a religious framework in this constant endeavor. Providing a meaning for the otherwise incomprehensible circumstances of personal tragedy is one of the major functions, raisons d'être, and appeals of religion. While the neurotransmitter hypothesis regarding the etiology of depression offers a rational scientific explanation for the occurrence of depression, it does not address the question "Why me?" in the personal terms in which we are accustomed to explain the events of our lives.

A recent review by Schiller and Levin (7) of the influence of religion on health care utilization points out that, while most studies have demonstrated significant religious differences in rates of utilization, simple interpretation of these results is confounded by failures to inquire beyond major religious group affiliation. Our purpose in this study was to begin to identify one of the various ways in which religious beliefs affect the way one views the causes of illness in general and one's own illness in particular.

Although physicians may not believe that questions of ultimate meaning fall within their purview or expertise, nevertheless it is clear that many psychiatric patients do think about such issues and that at least a substantial minority believe their own moral transgressions have played some role in the development of their illnesses. While physicians' opinions may differ as to the legitimacy, wisdom, and appropriateness of entering into a discussion with a patient about the moral significance of an illness, it has been our experience that most physicians provide their patients with a biological reductionistic explanation of the etiological mechanisms of disease and reassuringly gloss over the moral or transcendental import of the disease to the ill person and his or her family. Perhaps the physician needs to pay a little more attention to the patient's beliefs about causes of illness before hastening to a clinical explanation that fails to address the issues with which the patient is struggling.

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# Book Forum

## Nancy C. Andreasen, M.D., Ph.D., Editor

### NEUROLOGY

**Advances in Contemporary Neurology,** *edited by Fred Plum, M.D. Philadelphia, F.A. Davis Co., 1988, 204 pp., $45.00.*

This book has a vague title and for a good reason: its six chapters are a hodgepodge of topics lacking any unifying theme other than that they have to do with neurological diseases.

Although the book is obviously written for neurologists who like to be updated (but are not fussy about the topic), psychiatrists can find parts of it useful. Some chapters (two, three, and five) are to be tasted, others (one and four) are to be swallowed, and only one (chapter six) is to be chewed and digested.

Few psychiatrists would be interested in the post-polio syndrome (chapter 2), mitochondrial myopathies and encephalomyopathies (chapter 3), or tuberculosis of the central nervous system (chapter 5), save, perhaps, for those who may get consulted for the psychiatric complications of those neurological diseases. Except for a brief allusion to the psychosocial aspects of the post-polio syndrome, there is no mention of the psychiatric sequelae of these disorders.

On the other hand, the neurological complications of acquired immune deficiency syndrome (AIDS) and human immunodeficiency virus (HIV) infection (chapter 1) is a timely topic that would be of interest to quite a few psychiatrists. Although this chapter is well written, numerous articles have appeared over the past year in this area (particularly regarding the cognitive changes of interest to psychiatrists) that make this review of progress somewhat dated. Chapter four, on the selection of anxiolytics in clinical neurology, could have been of great interest to many psychiatrists. However, this chapter, although very readable, is actually too elementary to serve as an update on anxiolytics for the practicing psychiatrist and would be more useful for a medical student or a junior psychiatric resident.

The most interesting chapter, in my opinion, is that on evolving clinical concepts regarding the prefrontal-limbic systems (chapter 6). Schizophrenia researchers as well as neuropsychiatrists would find this chapter highly relevant because of the emerging roles of the dorsolateral prefrontal cortex and the frontal-limbic systems in understanding the pathophysiology of schizophrenia and related disorders.

Finally, with regard to the general usefulness of books such as this, I think that physicians who read selected data papers or review articles in good journals on a regular basis get a better return for their time and money than those who buy a book composed of several unrelated overview articles of diverse interest. I should add, however, that the chapters in this book are obviously well written and very well referenced.

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### SUBSTANCE ABUSE

**Getting Better: Inside Alcoholics Anonymous,** *by Nan Robertson. New York, William Morrow & Co., 1988, 298 pp., $17.95.*

Alcoholism is an exceedingly common disorder. The Epidemiologic Catchment Area study, which evaluated a general population sample of nearly 20,000 adults in five sites, established a lifetime prevalence for alcohol abuse or dependence of 13.7% for adults in the United States (1). Of those subjects who met *DSM-III* criteria for alcohol abuse and/or dependence, nearly half also fulfilled criteria for a second psychiatric disorder. It seems that psychiatric "dual diagnosis" is also a very common condition. A historical perspective, however, reveals that among physicians in general and psychiatrists in particular, interest in alcoholism is a relatively recent phenomenon. With the growth of medical concern about alcoholism, an increasing number of professional books and journals have focused on aspects of alcohol problems and their treatment. Even more numerous have been the books and magazines directed at various segments of the public: the millions of people suffering or recovering from alcoholism, the many family members living and coping with the disease, and the additional millions of adults who are children of alcoholic parents, trying to sort out the effects of their parents' illness on their own lives.

One such publication is Nan Robertson's very personal yet wide-ranging book *Getting Better: Inside Alcoholics Anonymous.* Robertson is a *New York Times* reporter who won a Pulitzer Prize for her first-person account of a bout with toxic shock syndrome. She is equally open about her struggle with alcoholism and her recovery, including a hospitalization for depression after a year and a half of sobriety and her successful psychiatric treatment. However, this book is not primarily about Nan Robertson's illness. Instead, it presents an insider's view of recovery, including a patient's-eye view of an alcoholism rehabilitation unit and an international tour of Alcoholics Anonymous (AA) and Al-Anon meetings. The book also describes the history and development of these remarkable self-help groups, the form and content of their meetings, and the role of spirituality in their programs. There is a chapter about the disease concept of alcoholism, including highlights of current physiological and genetic research. Finally, there is an appendix on how to recognize the symptoms of alcoholism and how to find help.

The book maintains a lively and engaging style, providing a firsthand account of the travels, readings, and interviews that yielded the book's basic information. Robertson opens with an interview with Lois Wilson, co-founder of Al-Anon and wife of the co-founder of AA, and goes on to quote many recovering alcoholics, medical authorities, and AA old-timers. Robertson successfully avoids idealizing AA by presenting some of the organization's problems as well as its strengths. Best of all, she captures some of the humor and humanity of AA while avoiding any sense of competition between AA and professional treatment.

This book is written for a general audience and would be quite appropriate to recommend to alcoholic patients and families. Patients who have misconceptions about these groups or fear that they are religious cults will be helped to accept referral. For the professional who has little experience with the 12-step movement, the book will also provide a good introduction, although nothing can quite equal the experience of attending open meetings. Every psychiatrist should do so.

As Ms. Robertson points out, organized medicine has not always been friendly to AA. A 1939 *JAMA* review of *Alcoholics Anonymous* (2), now generally called the "Big Book," stated, "The one valid thing in the book is the recognition of the seriousness of addiction to alcohol. Other than this the book has no scientific merit or interest." Fortunately, subsequent events have led to a far more cooperative relationship between medicine and AA, with great benefits to both sides. Ms. Robertson, through her own recovery and through her carefully written book, is living proof of these benefits.

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**Alcohol and the Writer,** *by Donald W. Goodwin, M.D. Kansas City, Mo., Andrews and McMeel, 1988, 210 pp., $16.95.*

Not everyone may know that Dr. Goodwin, accomplished psychiatrist and chairman of his department at Kansas, began his professional life as a journalist in New York City. After college and before medical school, he wrote feature columns for a syndicated newspaper. Medicine is his second career. After reading *Alcohol and the Writer,* one appreciates how talented he is in both fields.

The thesis of this book is that the American writer in the first half of this century was extraordinarily susceptible to alcoholism. Epidemiologic data on the relationship between writing and alcoholism have been explored by other authors, most notably Andreasen (1), with convincing results: creative writers are at greater risk for alcoholism. Goodwin does not establish this relationship with systematically collected epidemiologic data but makes the point by noting that four of the six American writers awarded the Nobel Prize in literature were clearly alcoholic (Sinclair Lewis, Eugene O'Neill, William Faulkner, and Ernest Hemingway). The fifth laureate, John Steinbeck, drank very heavily and would probably meet the criteria for alcoholism. If Steinbeck is included, this represents a rate of alcoholism of over 80%. The remaining American Nobel laureate is Pearl Buck, who Goodwin suggests might not have deserved the prize anyway. Goodwin further demonstrates the association between writing and alcoholism by developing a list "off the top of the head" of 48 famous American writers known to be alcoholics. The thesis seems valid: there was an "epidemic" of alcoholism among famous writers in the United States during the first half of this century.

Goodwin explores a number of questions about this epidemic. Did it involve only American writers? Was it confined to the first half of the present century? Did the epidemic include creative people in other arts? Did it affect only well-known writers? Did it involve specifically alcohol or were other drugs also abused? Rather than summarize Goodwin's conclusions on these issues, I will leave the reader of this review in suspense, to learn the answers by reading this fascinating book.

Goodwin searches for possible causes of alcoholism among creative writers. The first he considers is that "the hours are good." That is, the occupation of writing does not require specific hours, and the author's family, friends, or agent cannot easily check up on whether he or she is actually writing when sequestered in the study at any particular time. The writer may in fact be drinking, daydreaming, or both. Goodwin contrasts this with the postman's schedule. Who could get up at dawn and tote a heavy mailbag from door to door for hours while suffering from a hangover? Goodwin notes that postmen have a very low rate of alcoholism.

The second hypothesized cause is that heavy drinking is expected of writers. Twentieth-century American society may expect drunkenness of its famous men of letters, an idea consonant with the romantic image of the writer as a tragic, lonely, and doomed figure. The flaw of drunkenness is in keeping with the notion of romantic despair.

Goodwin's third possible cause is that writers derive inspiration from drink. There is disagreement on this point among writers themselves. However, Goodwin provides evidence that many writers believe alcohol facilitates the creative process and that some even believe it is essential to it.

Goodwin puts the most emphasis on a fourth possible cause, which he terms "the loner theory." Relying on biographies of famous writers, he notes that the themes of loneliness, shyness, and isolation recur frequently in these creative individuals. These traits are also common in alcoholics. Both alcohol and writing may assuage these feelings—alcohol through its disinhibiting effects and writing because this process allows authors to communicate with the characters they create. Further, creative writing requires a rich fantasy life. Loners often have a rich fantasy life, and alcohol promotes it. These traits of isolation and difficulty in communicating with real people may relate to the high rates of affective illness also reported in creative writers. Other intriguing possible causes are described, some proposed by alcoholic writers themselves.

In addition to his exploration of the causes of alcoholism in writers in general, Goodwin provides a detailed exploration of salient causes in particular authors. In a chapter on Faulkner, for example, the role of heredity is stressed. William Faulkner was the fourth generation of "heavy drinkers." At least two generations of Faulkners had periodic stays in an "institute" in Memphis to "take the cure." William Faulkner's three brothers were all given to drink in a big way. A chapter on Eugene O'Neill focuses on the role of his Irish cultural background, a culture that sanctioned and encouraged the medicinal use of alcohol for ills of the mind, body, and soul. The maid in O'Neill's autobiographical *Long Day's Journey Into Night* says that "a drop now and then is no harm when you're in low spirits, or have a bad cold." Eugene's father in the play agrees: "I've always found whiskey the best of tonics." O'Neill used alcohol in this manner. His introduction to this use of alcohol was early. In keeping with an old Irish custom, Eugene's father put drops of whiskey in his infant son's water as a palliative for nightmares and stomachaches. Other chapters explore the alcoholism of Edgar Allen Poe, F. Scott Fitzgerald, Ernest Hemingway, John Steinbeck, Georges Simenon, and Malcolm Lowry.

Alcoholism among writers is the focus of this book. However, Goodwin's treatment of these writers goes beyond this issue. In a few pages he provides insights into these fascinating personalities as revealed by their own words, their effects on others, and revealing episodes from their daily lives. We see Hemingway arriving in New York after a long stay in Cuba; he is restless, competitive, and obsessed with comparing himself to other writers. Goodwin describes him as counterphobic, overcoming fear by acts of courage. We get a feel for F. Scott Fitzgerald, drinking his turbulent way through the 1920s with Zelda, his life ending prematurely and tragically in Hollywood in 1940.

This is a book to be read leisurely. Insightful and fascinating, and written in a charming manner, it delights as well as informs.

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**Assessment and Treatment of Addictive Disorders,** *edited by Timothy B. Baker and Dale S. Cannon. New York, Praeger, 1988, 320 pp., $49.95.*

The critical reader will question why a collection of eight seemingly unrelated contributions should be bound into a volume. In the well-written introduction, the editors present a clear rationale for assembling these articles in a book. Their basic assumption is that disorders such as alcoholism, smoking, heroin dependence, and eating disorders are more similar than different. There is a theoretical basis for this viewpoint, but it has yet to be proven as conclusively as the editors imply. In this respect, the book represents the far too prevalent and rather simplistic current trend of indiscriminately lumping under the rubric of addictions the psychoactive substance use disorders along with several other behavioral problems involving excesses.

The editors have divided the articles into two sections: Assessment and Treatment. This simple organizational scheme seems artificial and somewhat contrived when one recognizes that most of the papers do not really adhere to it. The authors describe their research projects involving both assessment and treatment of the disorders with which they are dealing, and rightly so, because in practice, assessment and treatment are inexorably intertwined.

It may be of some value to summarize the major topics covered in each paper. Maisto et al. discuss how the drinking pattern of alcoholics can be characterized in terms of prototypic drinking profiles over time and speculate about associations of these profiles with personality type, etiologic factors, and response to treatment. Kirschenbaum presents the theoretical basis of cognitive therapies for addictive disorders. Under the rubric of self-regulatory failure, he enumerates those processes he considers important to the maintenance and generalization of behavioral change. Annis and Davis describe the development and use of two questionnaires for alcoholics that attempt to evaluate the threat of relapse posed by high-risk situations for which the patient has no effective coping response. Humphrey's discussion of the relationship between family processes and the psychopathology of patients with bulimia concludes the Assessment section. Humphrey highlights some of the similarities between deficits in bulimia and related patterns in various chemical addictions.

The editors describe the Treatment section as "admittedly parochial in that it contains two [of four] chapters on aversion therapy." Pairing the taste and smell of an addictive agent with malaise is reproducibly associated with the acquisition of a taste aversion. These data are generalizable because they have been replicated by Cannon et al. for alcohol and by Tiffany and Baker for cigarette smoking. It should be pointed out that there is no good evidence to indicate that aversive therapies produce long-term outcomes superior to those achieved with nonaversive strategies and that aversive therapies are currently out of favor among those who are in the mainstream of the treatment of psychoactive substance use disorders. The contribution of Brandon et al. deals with the beneficial effects of maintenance treatment; these authors contend that modern smoking cessation programs, which often have very high initial cessation rates, need to be complemented by extended treatment to prevent relapse. These observations are probably applicable to other psychoactive substance abuse disorders and suggest that we may be placing undue emphasis on "treatment programs" and insufficient attention on the "aftercare" components of the treatment. Hall et al. discuss another relatively neglected area—the extratherapeutic social and vocational aspects of treatment—in their chapter on job training programs for heroin addicts. Issues that are not typically involved in psychotherapy can be demonstrated to be of considerable relevance to the long-term functioning of patients with psychoactive substance use disorders.

The editors admit that

> this book does not constitute a broad review of assessment and treatment approaches to addictive or habitual disorders. Rather, we have solicited contributions that we believe represent promising approaches to addiction assessment and treatment and that report complex data sets on relevant topics. We asked all contributors to incorporate their own data into their chapters. We believe that this promoted specificity of exposition that should make the chapters more valuable to the reader.

Without question, the individual articles are scholarly, but they are so directly focused on the writers' research interests that they may be of limited value to the generalist. Even the psychiatrist who specializes in the area of alcoholism and substance abuse might find this book tough going. I was left with the opinion that the discussions in this book were strange bedfellows and that they would have been more appropriate for various specialized journals, where they might have been published in abridged fashion for the consumption of researchers rather than clinicians.

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**The Chemical Brain: The Neurochemistry of Addictive Disorders,** *by Sidney Cohen. Newport Beach, Calif., CareInstitute (Comprehensive Care Corp.), 1988, 100 pp., $8.95 (paper).*

Whoever invented the term "role model" must have had Sidney Cohen in mind. With his white mane of hair and handsome features, he sparkled with good will, humor, and common sense.

In his preface to *The Chemical Brain,* David Smith says that Cohen was the "most rational voice" in the irrational world of drugs. He was the field's elder statesman. He challenged extremism of every variety and was a pioneer in the scholarly inquiry into the causes and treatment of addictive disease. "Sidney Cohen took the long view and tempered scientific objectivity with humanism. He was a great source of knowledge, inspiration and guidance, and he will be profoundly missed." Cohen died in 1987.

Robert L. DuPont, in *his* preface, sees Cohen as the "trusted wise man in a field filled with lots of smoke but little light. No one else, literally, could think and write the way Sidney Cohen did. No one else commanded such broad respect from the most prodrug to the most antidrug zealots . . . he was a man without enemies in a field filled with hostility."

Cohen probably would not have been pleased by the 1989 Supreme Court decision that custom agents and rail workers should receive urine testing. There are many ways, he said, to dupe urine screening. "I am not sure urine testing will identify drug use, but it will detect stupidity."

Cohen received a degree in pharmacy in 1930 and a bachelor's degree from City College in New York in 1932. He got an M.D. in Bonn, Germany, in 1938. He studied LSD before hardly anyone had heard of it. He debated Timothy Leary and took a dim view of marijuana. He was a researcher, a teacher, a clinician, and a bureaucrat by turns, bringing distinction to each role—grounds for the fine *in memoriae* written by his friends Smith and DuPont.

Before his death at 76, Cohen worked on the present book with great enthusiasm. His aim, he said, was to "summarize the current state of knowledge about the way the brain worked, using new scientific knowledge to explain drug abuse." He succeeded. *The Chemical Brain* is not only his last book, but his best.

Cohen begins,

> On the autopsy table we see a three pound, pink-gray, nondescript, gelatin-like mass. Except for a number of wrinkles and bulges it could be something that had been prepared for eventual breadmaking. Its electrical production is trivial. Harnessing the entire central nervous system's electrical output could hardly light up a 20 watt bulb . . . . As recently as a dozen years ago, little of what is written here was known or even imagined.

Although it does not deny the importance of cultural factors, this book is almost entirely about biochemistry. Dr. Cohen's aim was to produce "neither a primer for beginners nor a treatise for the researcher, but rather a simple volume for the health professional and for the lay person with some basic information or interest in biochemistry." Technical language was unavoidable, but a glossary is provided.

Cohen starts with the neuron, goes on to neurotransmitters, and then launches into the chemistry of addiction, dealing with substances one by one. In 10 pages he covers the genetics of substance abuse and in another dozen pages talks about the imaging of the brain. There are scattered figures and tables to help the reader, but the charm of the work lies in the prose, which is simple and concise in the way that Cohen's newsletters are remembered by his readers. An enormous amount of information is crammed into these pages, yet the book will probably be used for reference more than for straight-through reading. Cohen practiced economy in his writing, rarely seen in works by even the better science journalists, and he is not only clear but authoritative.

Sidney Cohen will be missed.

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## ANXIETY

**The Nature and Treatment of Anxiety Disorders,** *by C. Barr Taylor, M.D., and Bruce Arnow, Ph.D. New York, Free Press, 1988, 415 pp., $35.00.*

If this is indeed the age of anxiety, the past 10 years could be characterized as the decade of anxiety research. Recent surveys have shown that 8% of the adult population may be suffering from serious anxiety disorders during any 6-month period, and more than 80 million prescriptions for antianxiety drugs are written each year in the United States alone. Most physicians, including some psychiatrists, appear confused by the knowledge explosion and the many different approaches toward understanding and treatment.

This volume is one of those rare books which come along at a time when they are most needed. It is coherent, comprehensive, and clinical. Its coherency derives primarily from continuity of authorship. The same style, tone, and fluency mark it as the work of a single mind with the help of a careful editor and collaborator. Both authors should be given great credit for the depth, breadth, and scope of their knowledge and ability to impart it to the reader. The book is comprehensive in the attention it pays to the many theoretical models while presenting a unified and unifying approach. It avoids pitting biological against psychological approaches. It includes one of the best discussions that I have read on the behavioral inhibitory systems. It is clinical in a very practical way, focusing on symptoms at the beginning of treatment and leading to approaches that involve more insight, understanding, and family therapy later on. The interspersed clinical cases are excellent and helpful.

I found the section on panic disorder particularly useful. The authors describe in great detail their sequential intervention techniques, which use education, diaries, change in life style, controlled breathing, cognitive strategies, and paradoxical intention. The authors provide a virtual blueprint for setting up a panic disorder clinic or program based on their experience with thousands of patients. The chapter on psychopharmacology is also excellent, as is the chapter on medical problems associated with anxiety. The extensive appendixes include the Stanford Agoraphobic Exposure Protocol, which is particularly useful for those who are involved in anxiety research. Therapists will find the case examples and the discussion very helpful in their own work as well.

This book is one of the best general textbooks on anxiety disorders that I have read. It highlights the importance of the biopsychosocial perspective, thorough assessment and evaluation, and practical guidelines for treatment. More than

400 pages are packed with new and useful information that should help reduce the anxiety of psychiatrists who are treating increasing numbers of patients with anxiety disorders. It will be a valuable reference for residents, medical students, and primary care physicians as well.

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**Handbook of Anxiety Disorders,** *edited by Cynthia Last, Ph.D., and Michael Hersen, Ph.D. New York, Pergamon Press, 1988, 598 pp., $90.00.*

The anxiety disorders are currently an area of active interest and research. Given the large amount of literature on the topic, it is timely, appropriate, and useful to try to produce a broad-based reference text in the area. This appears to be the editors' goal. They have drawn contributions from both psychologists and psychiatrists and have made a special effort to include chapters on all possible relevant topics. The results, although generally successful, are sometimes uneven, and each chapter has a different approach, writing style, and quality. The degree of deviation from mainstream thinking on a given topic also varies somewhat in each chapter, according to each author's approach. (There is nothing wrong with this, but readers should be aware of it.) There are a few minor editing problems, but these do not appear to be important.

The book is divided into seven sections. The first, Overview, consists of a brief introduction by the editors and an ambitious attempt by Jeffrey Gray to summarize available knowledge on the neuropsychological basis of anxiety. Various chapters in the second section, Clinical Features and Assessment, focus on the nosologic and phenomenologic aspects of the major anxiety disorders. The third section, Development and Maintenance, is interesting in the diversity of topics covered: genetics, animal models, pharmacologic models, psychophysiology, psychodynamics, stress and vulnerability, life events, and personality disorders and anxiety. Each of the chapters in this section is independent of the others. For example, the chapter on psychodynamics seems to have minimal connection to the other chapters. An attempt to integrate these chapters might have been worthwhile.

Section four, Psychological Treatments, is a series of interesting and clinically relevant chapters, each written from the position of a different school of thought. Section five, Pharmacological Treatments, includes a series of chapters on drugs used to treat anxiety disorders organized by drug classification (benzodiazepines, β-adrenergic blockers, tricyclic antidepressants, and monoamine oxidase inhibitors) as well as a chapter on combined pharmacological and psychological treatment. They are generally well written and clinically useful. The chapter on monoamine oxidase inhibitors by David V. Sheehan and Ashok B. Raj was an especial pleasure to read.

The sixth section, Special Topics, deals with areas where an attempt at comprehensiveness may have led to some unevenness. Often this is because there are few data available. The chapters on anxiety disorders in childhood and adolescence, anxiety in the elderly, and medical illness and anxiety are interesting and valuable. In the chapter on suicide and anxiety, the authors admit that there really is no literature but review the subject as best they can. The chapter on primary prevention of anxiety disorders does not appear to be tied down to clinically relevant anxiety disorders at all but, rather, turns into a political statement against violence in our culture and a plea for more federal funding of the authors' topic areas. Although I am not against these sentiments, they do not fit in easily with the more empirically grounded chapters. The last section of this book, Future Directions, contains one brief chapter with suggestions for further work in the field of anxiety.

Overall, this book appears to be a useful reference text best used by those who wish to get quick overviews of certain areas of anxiety disorders with which they are not already familiar.

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## BENZODIAZEPINES AND COUNSELING

**Benzodiazepines and Therapeutic Counselling: Report From a WHO Collaborative Study,** *edited by the World Health Organization. New York, Springer-Verlag, 1988, 135 pp., $55.90.*

Benzodiazepines are frequently prescribed by psychiatrists but are used even more extensively by nonpsychiatric physicians. Such widespread prescribing is not only a national but a global phenomenon. Is such widespread use therapeutically indicated? Are nonpharmacological treatments equivalent or safer? Attempts to answer these questions with a national focus have not been totally successful. To attempt to answer such questions from an international perspective is daunting. The monograph under review from the World Health Organization (WHO) reports on a collaborative study that attempted to assess the comparative value of benzodiazepines versus counseling in patients with "minor" psychiatric symptoms in four culturally distinct countries. The attempt is noteworthy, and the results are interesting.

The first chapter of this short monograph places the study in the context of other psychopharmacological studies being conducted by WHO. The second chapter reviews the world literature regarding cross-cultural comparisons of the effectiveness of psychotherapy and psychotropic drugs in general and benzodiazepines in particular. The review reveals mainly that research in this area is very sparse.

The third and fourth chapters describe the aims, materials, and methods of the study. In brief, the study sought to determine the efficacy of diazepam versus brief counseling "of a sort which might be given by a nonpsychiatrist in medical practice" when used to treat patients "with a wide range of minor physical and psychological symptoms." The 6–12-week study had a two-way factorial design with diazepam at two levels (present and absent) and counseling at two levels (present and absent). Four psychiatric centers were involved, located in London, Bombay, Tokyo, and Ibadan, Nigeria. Standardized rating instruments were used, and central training of researchers was accomplished. At some locations, the counselor was also the assessor; therefore, blindness to counseling was not maintained as it was for the drug groups. The General Health Questionnaire, the Present State Examination (PSE), and the Rating Scale for Side Effects were the main rating instruments. The amount and type of counseling administered were carefully recorded. The descriptions of the patient groups are interesting and highlight the difficulty of this type of research. For example, the Tokyo center was unable to enroll a sufficient number of patients for most analyses, which the authors speculated was due to patients in Japan being "very sensitive when treated experimentally . . . they seldom express this lack of confidence directly with the doctor but simply stop attending clinic."

Chapter five presents results. Given the diversity of the centers, the results were surprisingly consistent. The most powerful treatment was time; all centers reported marked improvement in all groups, as measured with all rating instruments, beginning at 2 weeks and continuing to grow to the 12th week. Using change on the General Health Questionnaire as the assessment instrument, the study demonstrated that patients in counseling in Bombay and London showed significantly greater improvement from the second week onward than patients not receiving counseling in these centers. Diazepam was of greater value than placebo only at Ibadan and only at week 2. With change on the PSE (which was administered only at baseline and week 6) as the assessment measure, counseling was superior to no counseling in Bombay and diazepam was superior to placebo in Ibadan. The latter finding was at the 0.05 level of significance, and the authors point out that it should be interpreted with caution given the multiple assessments that were made.

An evaluation of "treatment-emergent symptoms" (side effects) indicated that they were not very common and that patients who received neither drug nor counseling had the same incidence of side effects (including drowsiness) as those who received active treatments.

The sixth chapter, which analyzes the specific results of counseling, has some interesting findings. For instance, certain themes, such as work and illness or health, emerged as predominant issues in counseling (in terms of the proportion of time spent discussing them) at all four centers, but other themes, such as self-doubt, varied greatly among the centers. Other findings are difficult to interpret. For example, ventilation was the technique most widely used in London and Bombay, but "history taking" was the most widely used technique in Ibadan and Tokyo. However, these categories were confounded by nonuniform interpretation of their meaning at the four centers.

Chapter seven summarizes the study and discusses its methodological limitations. These include the low doses of diazepam used (6 mg for the first 2 weeks with possible increases to a maximum of 12 mg at week 12), nonblind assessments, and lack of uniformity in type and length of counseling.

What does this study tell us? Across diverse cultures, time (or, more precisely, time spent under a clinic's care) alleviates minor physical and psychiatric symptoms. The result of time is improved by the addition of counseling, at least in two of the cultures studied. Diazepam at the low doses used adds little, if anything, positive or negative, to these results. Therefore, the study implies but does not prove that the widespread international practice of using low-dose benzodiazepines for the treatment of minor physical and psychological disorders is unnecessary but not dangerous in the short term. Whether this implication is supported by the study can be debated, but the study does indicate the framework for addressing such issues.

In summary, the study demonstrates that multicenter cross-cultural studies, although difficult, are possible and of value in extending our knowledge of pharmacotherapy, psychotherapy, and their interactions in diverse cultures.

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## ETHICS AND LAW

**Morality: A New Justification of the Moral Rules,** *by Bernard Gert. New York, Oxford University Press, 1988, 306 pp., $34.00.*

This volume is an enlarged explication of a moral theory first presented by Dr. Gert in *The Moral Rules* (1). In the preface and introductory chapters, Dr. Gert explains why he revised the earlier volume. In fact, *Morality* is not only an enlarged version of *The Moral Rules* but also a result of two more unpublished revisions used in teaching. It is clear from cursory reading that Dr. Gert has reconsidered every word, every sentence, and every paragraph so that no material is extraneous or unjustified or casual.

Dr. Gert is Stone Professor of Intellectual and Moral Philosophy at Dartmouth and Adjunct Professor of Psychiatry at Dartmouth Medical School. His interest in psychiatry and problems of psychiatry is eminently clear, particularly in latter portions of the book, where he discusses such concepts as personality, character, psychic determinism, paternalism, and informed consent. He defines what he means by each of these commonly used psychiatric concepts, and his definitions are different from the typical psychiatric definitions. For example, in his discussion of personality traits he states,

> A personality trait primarily concerns feelings, not . . . action . . . since the normal pattern is for a person to act according to her feelings. Words which refer to personality traits are often mistakenly thought to apply primarily to dispositions to act. Describing someone as shy is often taken as saying something about her disposition to avoid meeting new people. But shyness, as a personality trait, is the disposition to suffer anxiety at meeting new people rather than the disposition to avoid them. This can be seen from the fact that we can say of someone who acts like a politician at election that she is really shy, but that she has overcome her shyness. It is not feelings themselves, but the disposition to have those feelings in certain kinds of circumstances that are the personality traits.

I have quoted this paragraph to provide a feel for Dr. Gert's literary style and to illustrate how his use of a common psychiatric term, "personality trait," differs from that of the average psychiatrist.

Dr. Gert presents his analysis of some of the more common philosophical concepts of morality, including rationality versus irrationality, good versus evil, impartiality versus partiality, and virtue versus vice. From these concepts and their relationships he develops a moral theory to describe and justify a common moral system. The essence of his moral theory attempts to answer the question, What is morality? He answers,

> Morality is a *public system* that applies to *all rational persons* insofar as their behavior affects others, its goal is the *minimization of evil suffered,* and the moral rules form a central part of it. A justified moral system is one that all *impartial, rational persons,* using only those beliefs that are shared by all rational persons, would advocate adopting as a *public system* that applies to all rational persons.

From this summary definition, Dr. Gert develops 10 moral rules: 1) don't kill, 2) don't cause pain, 3) don't disable, 4) don't deprive of freedom, 5) don't deprive of pleasure, 6) don't deceive, 7) keep your promise, 8) don't cheat, 9) obey the law, and 10) do your duty. He justifies these moral rules and designs a moral system with various examples that expand on the simple moral rules.

Dr. Gert elaborates a moral attitude which suggests that a moral rule must always be obeyed except when "an impartial, rational person can advocate that violating it . . . be publicly allowed." Again, he provides illustrations. From moral rules come moral ideals that "cannot be obeyed impartially. Twenty-four hours a day, seven days a week, fifty-two weeks a year." This differentiates rules from ideals because it is impossible to follow ideals. Finally, in the last chapter, Dr. Gert describes some applications of the moral system and discusses paternalistic behavior, active versus passive euthanasia, and what is a physician's duty.

At one point when writing about moral ideals, specifically about disease, Dr. Gert says, "When one is talking about disease it may be sometimes more appropriate to talk of the moral ideas of preserving life, relieving pain, and lessening disabilities." He then adds, "In former times, it was thought that these moral ideals were the primary motives for those who went into the practice of medicine, and so doctors used to be regarded as among the morally best persons." Unwritten, of course, is the thought that if doctors would only continue to adhere to these ideals their reputation and community regard might improve and they would once again be considered among the most moral persons.

This is not a book for the medical student, new psychiatrist, or casual reader. Although Dr. Gert is very careful in defining terms and concepts, his definitions require careful thought, analysis, reading, and rereading. The book does, however, manage to use the academic discipline of moral philosophy to answer real questions confronting physicians dealing with patients in real situations; it offers guidelines on which to base treatment decisions. I found the book original and interesting, and I expect to use portions of it to help do what Dr. Gert suggests—i.e., teach students. He says, "I have shown what morality is. Others are needed to teach people to follow it."

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**Informed Consent: Legal Theory and Clinical Practice,** *by Paul S. Appelbaum, M.D., Charles W. Lidz, Ph.D., and Alan Meisel, J.D. New York, Oxford University Press, 1987, 269 pp., $27.95.*

Most psychiatrists, when asked to think, read, or talk about medicolegal topics such as involuntary commitment, competency, and informed consent, automatically flinch and assume a paranoid stance. When asked to review this book my first thought was, "Why me? I'm not an expert. I'm really ill at ease with the intricacies of it all, and these legalities are a nuisance as far as caring for my patients." Fortunately, my second thought was, "Why not, maybe it won't be so bad and I may learn something." The authors, a psychiatrist, a sociologist, and a law professor, have pooled their experience, research, and wisdom and written a book that is wonderfully free of jargon and clearly shows that "the requirements of informed consent can be met in a manner that improves, and does not impede, patient care." The book is exceptionally well organized, clearly written, and thorough; it is also a resource for further study because it is fully referenced.

The first two parts lead the reader through the ethical principles underlying the concept of informed consent and the historical development of law relating to informed consent. The ethical theories that are related to the principle of autonomy are detailed, and their strengths and weaknesses are nicely delineated in relationship to the conflict that clinicians experience daily. This conflict exists between truly allowing the patient full autonomy to make decisions about his or her treatment and our concern for the patient's health when the patient, for whatever reason, makes a decision that we feel is detrimental to his or her health. The authors present both sides of the arguments for the value of health versus the value of autonomy and allow the reader to struggle and reach a personal position based on a broader understanding of the underpinnings of informed consent.

The chapters on the development and current status of law regarding informed consent are thorough, clearly relate to the previous chapters, and provide the reader with an appropriate perspective and understanding of the law. The authors specifically state that "the law in many states is so vague as to provide no guidance." However, they provide readers with the concepts necessary to guide their actions in relation to patients. The chapters on exceptions to the legal requirements and competency are particularly good at establishing that there are no absolute legal guidelines and then providing a broad understanding of the issues involved. The authors provide a basis for understanding and applying the principles of informed consent to the patient that goes beyond the enumeration and translation of specific laws, codes, and regulations.

The last half of the book deals with the clinical application of informed consent and the tough decisions physicians and patients face together daily. The authors develop their thesis that the principles of good medical care and the principles of informed consent are not in opposition but are mutually reinforcing. They feel that physicians must be comfortable with the right of patients to participate in making medical decisions about their care and the sharing of necessary information with patients to allow their adequate participation in these decisions. They feel this interchange is an essential part of the "doctor-patient dialogue that lies at the core of an effective therapeutic relationship." They delineate informed consent as a process that occurs throughout the care of the patient, not as an event that occurs when a form is signed. Specific chapters are devoted to consent forms, patients who refuse treatment, and the difference between consent to treatment and consent to research.

The authors, instead of causing me to flinch, enabled me to be more expert and comfortable about informed consent and, no longer seeing it as a nuisance, to better apply the principles of informed consent in my work with patients. It is appropriate reading for all physicians who seek to improve their skills in establishing an effective therapeutic relationship.

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## DISORDERS IN THE ELDERLY

**Communication and Cognition in Normal Aging and Dementia,** *by Kathryn A. Bayles, Ph.D., and Alfred W. Kaszniak, Ph.D., with the assistance of Cheryl K. Tomoeda, M.S. San Diego, College-Hill Press (Little, Brown and Co.), 1987, 368 pp., $29.50.*

The central aim of the authors of this book is to present and defend the thesis that semantic memory is especially impaired in dementia and that impairment in semantic memory is the basis for problems in communication which develop in the various dementias. They define semantic memory as "the highest-level cognitive modality . . . consisting of concepts, propositions, and schema; . . . the aspect of the mind wherein ideation and inferencing take place; . . . the central processing unit of human knowledge, . . . particularly impaired in Alzheimer's disease."

The authors view semantic memory as "a store that contains concepts, but not their lexical representation." They postulate, therefore, that "concepts and words do not have a shared representation in neuronal circuitry." Thus, persons with dementia "have trouble producing linguistic information because they have trouble thinking, generating, and ordering ideas." Along with this, linguistic comprehension suffers because demented persons have less of a capacity to form expectations, make inferences, and distinguish given and new information. The authors note that dementia patients "suffer impairment in the ability to communicate while retaining considerable knowledge of language . . . . Dementia patients process word forms, syntax, and phonology, but not meaning and use." They make a clear distinction between the communication problems in the various primary dementing diseases and the different forms of aphasia observed with focal cerebral lesions. They found very similar problems in communication in patients with different dementing disorders, such as Alzheimer's disease, Huntington's disease, and Parkinson's disease. In patients with mild to moderate Alzheimer's disease, they caution that clinicians should anticipate greater problems in the ability to communicate than in speech or language.

The authors present a mass of data in support of their thesis, and their arguments are compelling. Unfortunately, the material is brought together in a very long book, which for the most part is difficult to read (as the authors frankly warn). In part this derives from the nature of the subject matter and from its unfamiliarity to those outside the fields of linguistics and aphasiology. It is also a result, however, of an attempt to include too much data, repetitiveness, and, sometimes, faulty organization. The book would have benefited greatly from a very critical editor. The references at the end of each chapter are unusually complete and valuable, and the glossary at the end of the book is most helpful.

In short, this is an important and valuable book in which the authors argue their postulates forcefully and back up their arguments with masses of detail. It will probably become required reading for scholars in the field. It is not, however, a book for the casual reader or for the fainthearted.

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**Psychosis and Depression in the Elderly: Psychiatric Clinics of North America, vol. 11, number 1, March 1988,** *edited by Dilip V. Jeste, M.D., and Sidney Zisook, M.D. Philadelphia, W.B. Saunders Co. (Harcourt Brace Jovanovich), 1988, 277 pp., no price listed.*

This is a work whose time has been long due. For years, older patients with depression and especially older patients with psychosis have been ignored, even though there are several important questions to be addressed from both clinical and research perspectives. These issues are even more important with the advent of a Board examination for added qualifications in geriatric psychiatry. The editors of this book have done an admirable job of compiling a series of useful chapters.

The first chapter, by Dilip Jeste et al., reviews the concept of late-onset schizophrenia. You cannot have a book on a subject if there is no subject. Indeed, these authors conclude after a careful literature review that there is evidence for late-onset (after age 45) schizophrenia. The following chapters progress in a logical sequence, discussing possible risk factors for the development of late-onset psychoses, late-life psychoses and neuroimaging, and neuropsychological correlates of late-life psychoses. These chapters discuss in some detail the neurochemical rationale for psychoses in older age, which is linked to a particularly interesting chapter discussing dopaminergic transmission in both psychoses and movement disorders in the elderly. These chapters represent essentially the only compendium of literature on late-life psychoses and as such are unique and valuable.

The rest of the chapters relate to affective illness in the elderly. This area has received much more attention than have psychoses in the elderly; therefore, the authors' task might be more challenging, at least in terms of the number of works to review. Yet the different authors respond to the challenge not only by reviewing more traditional areas but also by covering relatively new topics that are clinically relevant. A good example is the chapter by R. Yassa et al. on the elderly patient with bipolar disorder. As I sit writing this review I have a patient who is 67 years old, too medically ill with cardiac disease for ECT, floridly manic, in four-point restraints. Virtually every medication makes him worse. This book provides insights into such patients as well as technical references regarding the pharmacological nuances of their successful treatment. Of particular use are the chapters on drug interactions in the elderly, which list common problems in detailed but well-organized and easy-to-read tables. Such information might be of use to nursing staffs as well as treating physicians. All in all, I can recommend this work very highly.

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*Reprints of Book Forum reviews are not available.*

## Anabolic Steroid Dependence

SIR: Over the last two decades, some athletes have used androgenic anabolic steroids as an adjunct to weight training and exercising to improve their strength and physique (1). This practice came to international attention during track and field competition in the 1988 Olympics. Athletes continue to use these drugs in spite of numerous known side effects, including changes in libido, testicular atrophy, major psychiatric symptoms (2), abnormal results on liver function tests, cholestatic hepatitis, liver tumors, atherosclerotic heart disease (3), and changes in cholesterol metabolism. Brower et al. (4) reported a case in which a noncompetitive weight lifter's dependence on anabolic and androgenic steroids met the *DSM-III-R* criteria for psychoactive substance dependence. We report a similar case, which prompted us to wonder whether such cases will become more commonplace in chemical dependency units.

Mr. A, a 22-year-old white man, came to our chemical dependency unit stating that he could not stop taking steroids. He said that he had been a weight lifter for 2 years and was contemplating competitive lifting. His main complaints were depression and inability to stop his steroid use. He had no psychiatric history or other substance abuse history.

Mr. A had begun to use steroids 9 months before admission to the unit, in an effort to improve his weight lifting. His weight had increased from 175 to 218 lb, and he was able to bench-press 60 more pounds than he had previously. Initially, he established a cycle of taking the drugs for 4 weeks and then not taking them for 4 weeks, but he always felt that he should be "a little bigger." Therefore, he started decreasing the steroid-free intervals. Shortly thereafter he began adding parenteral steroids to his regimen of drugs taken by mouth. At the time of admission, Mr. A was training 6 days a week and had not stopped taking steroids for more than 2 weeks at any time in the past 6 months. His regimen included 1) oxandrolone, 25 mg/day, 2) nandrolone phenpropionate, 3) testosterone cypionate intramuscularly each week, and 4) methandrostenolone. The patient admitted having had a drug injection 4 days before his hospitalization. While taking these drugs, Mr. A complained of feeling depressed, sleeping less, and lacking energy; he described irritability with occasional temper outbursts that resulted in strained relations with his family. During the cycles when he was not taking steroids, Mr. A experienced steroid craving and decreased self-esteem, feeling that he was not becoming muscular fast enough. Therefore, he decreased these cycles and continued to "stack" his drugs.

A physical examination of Mr. A showed that he had hypertrophied muscles. Findings included acne over his back and chest (this began shortly after his steroid use) as well as a cardiac murmur and click, which had not been found on previous physical examination. He had a recent history of prostatic hypertrophy. His laboratory results showed a normal cholesterol level but slightly elevated triglycerides. His alkaline phosphatase level was minimally elevated.

Mental status examination revealed a dysphoric young man who was pleasant, cooperative, and questioning. He demonstrated no irritability or agitation. His thought processes were normal, and there were no hallucinations or delusions. He showed some preoccupation with body image, feeling that he was "not really all that muscular." He stated that he no longer felt in control of his steroid use.

Mr. A felt that he did not "fit in with the alcoholics and addicts" on the chemical dependency unit, but he participated actively in the program for 1 week, until he learned that his insurance coverage was inadequate, which prompted his leaving the hospital. His mood had improved prior to discharge.

This case suggests a diagnosis of psychoactive substance dependence much like that described by Brower et al. (4). Our patient estimated that 80%–90% of the bodybuilders and power lifters at his local fitness club were anabolic steroid users. Buckley et al. (5) reported that 6.6% of male 12th-grade students in a nationwide survey used or had used anabolic steroids. With the increasing prevalence of this problem, we may begin seeing more anabolic steroid abusers on our chemical dependency and psychiatric units. Specific detoxification and treatment strategies should be developed to address steroid dependence and the concurrent issues of low self-esteem and body image distortion.

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## Attending the Funeral of a Patient Who Commits Suicide

SIR: Psychiatrists constantly face the threat of patients' suicide (1). With one exception (2), the literature on therapists' response to suicide (1, 3–5) has failed to address the benefit or propriety of the psychiatrist's attending the funeral of a patient who commits suicide. I therefore report my own recent experience.

> Mr. A, a 27-year-old unmarried, unemployed man with chronic paranoid schizophrenia, jumped from a rooftop while in the throes of worsening psychosis. Seeing him some 30 hours earlier, I had felt that he would recompensate as an outpatient, as he had several times before, if he took a higher dose of neuroleptic. He complied with the increased dosage and yet still committed suicide. I had treated Mr. A for nearly 6 years, from the beginning of my second year of residency. In continuing to see him monthly after finishing my training, I had accepted treating him as a lifelong responsibility. Having expected to grow old with him, I found his suicide all the more difficult to abide.
>
> On learning of his death, I met with the patient's mother to help her grieve, explain the clinical issues, and express my own sorrow. A senior colleague had suggested that I attend the funeral—a thought I might otherwise not have considered. The mother mentioned the funeral and welcomed my coming. On arrival I was specially greeted outside the funeral parlor by the patient's sister and escorted to the body and the mother. It was a small, sad ceremony attended by older relatives. My patient had few friends; no one his age was there. In the open casket he appeared almost alive, showing no signs of the fall and seeming likely at any moment to breathe and rise. The family was grateful that I had come, and a respectful whisper swept the room: "The doctor!" I felt the sense of honor bestowed on our professional predecessors who attended when they could not cure.
>
> My attending the funeral seemed to benefit the family. I reassured them that Mr. A had not considered suicide when he was feeling well (which did not seem a breach of confidentiality in this circumstance). I offered ongoing support, which two family members accepted. Attending certainly helped me to mourn and "work through" the suicide (4). The ritual eased laying to rest not only the patient but my guilty retrospection about the treatment. I recognized how unique our relationship had been for Mr. A. I left less angry at myself and more enraged at schizophrenia. I saw the effect of the disease on mourners whom I knew well through the patient's descriptions but had not previously met. We survivors experienced the commonality of loss.

Is there risk or impropriety in attending a patient's funeral? In some instances the presence of a psychiatrist might betray a patient's trust, exposing an undisclosed relationship to family and friends; or a family might object. Neither was true in this case. I would generally recommend attending a patient's funeral as therapeutic for both therapist and family and as a hallowed, honorable extension of the physician's role.

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## Self-Mutilation in Combat-Related PTSD

Sɪʀ: In their interesting article "Self-Cutting After Rape" (1), Gail S. Greenspan, M.D., and Steven E. Samuel, Ph.D., invited additional reports of such patients. I wish to report instead the onset of self-cutting after a different kind of psychological trauma.

> Mr. A, a 43-year-old two-tour Vietnam veteran, developed severe chronic posttraumatic stress disorder (PTSD) after repeated intense combat. He gave no history of prior psychopathology. His current symptoms included intentionally burning his arms on the edge of his wood stove and inflicting superficial cuts on his hands with his hunting knife (accompanied by little or no pain), especially at times of intrusive recollections. He did this in order to break through a disturbing sense of numbness and "make myself feel something." His forearms showed burn and cut scars. He dated his self-mutilation to life-threatening situations in Vietnam, which were accompanied by feelings of floating above his own body. While firing his machine gun, he had noticed that he did not feel the red-hot shell casings landing on his exposed skin. During breaks in the action, or after it was over, he would burn himself with his cigarette lighter or cut himself in an attempt to get in touch with reality.

I do not recall previously encountering self-mutilation in combat-related PTSD, but I have not routinely inquired about it. Its occurrence in this case argues that it may be a general (though hardly ubiquitous) characteristic of PTSD, rather than a product of only one type of trauma (i.e., sexual). Mr. A's case is entirely consistent with Drs. Greenspan and Samuel's assertion that the cutting represents an attempt to end feelings of depersonalization, but it is not very consistent with the psychodynamic explanation of suppressed rage turned inward.

My colleagues and I have found naloxone-reversible diminution of pain sensibility in PTSD veterans after they viewed a combat videotape (2), which we interpret as reexperiencing of opioid-mediated stress-induced analgesia (3). Van der Kolk and Greenberg (4) proposed that endogenous opioids may be implicated in self-mutilation. The case presented here, and other cases of painless self-mutilation such as those presented by Drs. Greenspan and Samuel, suggest that beyond its occurrence in the laboratory, stress-induced analgesia may be a phenomenon of clinical significance in PTSD. The choice of the word "numbing" in *DSM-III-R* to describe a cardinal symptom of this disorder may not be coincidental.

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## Trazodone for Bowel Obsession

SIR: Following the article by Jenike et al. on the treatment of bowel obsessions with tricyclic antidepressants (1), two case reports (2, 3) pointed to the usefulness of the serotonergic clomipramine in treating the condition. I would like to report the dramatic response of a patient with bowel obsession to treatment with trazodone, a more readily available serotonergic antidepressant.

Mr. A, a 66-year-old retired man, was referred to my clinic by his internist because he had bothersome gastrointestinal complaints for which no physical basis had been found despite an exhaustive work-up. The patient had first experienced vague abdominal discomfort, occasional epigastric pain, and hesitation in swallowing during his service overseas in World War II. The symptoms had persisted over the years, although they had not interfered with his ability to work diligently as a clerk, marry, and raise five children successfully. About 20 years ago, however, he began to lose weight gradually and rather imperceptibly, although there was no change in his appetite. When he sought medical help, his weight was down to 120–125 lb from a premorbid 160 lb. After a thorough work-up with no abnormal findings, he was started on a daily Ensure supplement, which stemmed the weight loss but did not affect his complaints.

A psychiatric examination revealed that Mr. A had retired at age 55 because his symptoms were bothersome. He was leading a life of quiet leisure and showed no clinical evidence of depression, although he admitted to a chronically nervous disposition. He denied any obsessive-compulsive symptoms except for his constant battle with and fear of constipation. Mr. A worried incessantly about not being able to move his bowels regularly and connected this to his other gastrointestinal complaints. Over the years he had struck upon a rather novel ritual to which he succumbed only if he went without a bowel movement for more than a week or 10 days. He would walk into a local minimarket, and as soon as he entered the store, he would have an urge to evacuate and would rush back home. There was no family or personal history of other major psychiatric illness or substance abuse.

The patient was given a trial of trazodone because of my previous occasional positive experience with it for depressed patients with somatization. In 3 weeks Mr. A responded dramatically to a dose of 150 mg/day. His gastrointestinal symptoms remitted, his bowels moved regularly every 2–3 days, and he began to gain weight. After 6 months he continued to be well and weighed 145 lb. An attempt to reduce the dose of trazodone to 50 mg/day produced a return of constipation. I raised the dose to 100 mg/day and Mr. A responded again. Complete remission has persisted for the last 18 months. The Ensure supplement was withdrawn shortly after his initial response to trazodone.

The serotonergic effects of clomipramine have been linked to its usefulness in obsessive-compulsive disorders (4). However, Prasad (5) found that trazodone was more effective for milder obsessive symptoms. As Jenike et al. pointed out, bowel obsessions may be a circumscribed form of obsessive illness, and the efficacy of low-dose trazodone as well as tricyclics would thus point toward a more broad-spectrum pattern of response in this unusual condition.

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## Tardive Dyskinesia Associated With Molindone Treatment

SIR: Tardive dyskinesia associated with the use of molindone has only rarely been reported (1). I would like to add another case to that small literature.

Ms. A, a 29-year-old unmarried Caucasian woman, was admitted to a long-term treatment hospital for treatment of her borderline personality disorder and what had proved to be a refractory major depression. She had typical depressive symptoms, some history of alcohol abuse, suicidal ideation, a history of overdose attempts, and episodes of mild self-mutilation. She had had trials of multiple medications along with psychotherapy during five previous psychiatric hospital admissions, but her condition had deteriorated. She also had considerable anxiety and poor impulse control. Over the ensuing 22 months of hospitalization, in addition to expressive-supportive psychotherapy, the patient had received multiple well-controlled trials of various single antidepressants, attempts at lithium augmentation, and, ultimately, a combination of a monoamine oxidase inhibitor (MAOI) and a tricyclic. In virtually all of the medication trials, she showed some initial response but rapidly developed apparent tolerance and loss of benefit. Even with the transient improvements in mood, her anxiety remained untouched and appeared to be of psychotic proportions. Because of this, she also received brief trials of haloperidol, thioridazine, and thiothixene and, ultimately, molindone.

Results of Ms. A's neurologic examination upon admission were normal. At that time she was receiving phenelzine, 75 mg/day, and haloperidol, 10 mg/day. Lithium carbonate, 900 mg/day, was begun. After an increase of lithium to 1500 mg/day proved ineffective, lithium and phenelzine were discontinued and the dose of haloperidol was gradually raised to 25 mg/day. However, alterations in her menstrual cycle ensued, and her serum prolactin level proved to be quite elevated (95.5 ng/ml; reference range=0–14 ng/ml). A magnetic resonance imaging brain scan ruled out pituitary microadenoma, and her prolactin level returned to normal after haloperidol was withdrawn. The results of neurologic examination remained normal.

A series of trials of medication, including 1) nortriptyline, 2) nortriptyline and lithium, and 3) nortriptyline, lithium, and carbamazepine, failed, and Ms. A was started on a regimen of molindone, 25 mg b.i.d., which was gradually increased to 225 mg/day. Molindone was selected because of reports that it was less likely to cause tardive dyskinesia or to increase serum prolactin levels. Serial determinations of her prolactin level over several months showed that it remained normal. Meanwhile, there were additional trials of fluoxetine, doxepin, and clonazepam, none of which were successful.

By the 18th month of treatment, and after 3 months of taking molindone, typical oral-buccal-lingual masticatory movements, along with some akathisia, were noted when Ms. A was anxious. Her prolactin level had increased to 100 ng/ml, and the dyskinetic movements were constantly present. Molindone was then withdrawn. The patient agreed to begin taking an MAOI-tricyclic combination, with benzodiazepines for her anxiety, which proved at least partially effective.

Three months after withdrawal of molindone, the oral-buccal-lingual movements were becoming less severe and less constant, and after 6 months they had almost completely disappeared. However, Ms. A was then showing generalized anxiety punctuated by panic attacks, and she was given additional axis I diagnoses.

After 22 months of hospital treatment, Ms. A was discharged to a transitional program.

While this case is perhaps typical of others in which an association between molindone treatment and initial dyskinesia rather than tardive dyskinesia has been reported because other antipsychotic drugs were involved (2), the clinical presentation was that of bona fide tardive dyskinesia, which perhaps luckily resolved after withdrawal of molindone. Since molindone is a dopamine $D_2$ receptor site binder, it is not surprising that it produces these effects, despite its otherwise somewhat atypical behavior (3).

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## Possible Induction of Mania by Buspirone

SIR: Buspirone is an anxiolytic agent, chemically and pharmacologically different from other currently marketed antianxiety medications. Its anxiolytic effectiveness is comparable to that of benzodiazepines. Preliminary data suggest that it has some antidepressant properties (1, 2). We recently read with interest a report of buspirone-induced mania (3), and we present here the case of a patient in whom mania occurred shortly after initiation of buspirone therapy.

> Ms. A, a 32-year-old woman, had been given a diagnosis of bipolar disorder when she was hospitalized for mania 10 years ago. Since that time she had remained stable as an outpatient, with no recurrence of mania, but had had several episodes of depression. She had required no psychotropic medication for the past 2 years, during which time she had been treated with weekly psychotherapy. She began developing prominent anxiety while making arrangements to resume her career and was started on a 15-mg/day dose of buspirone. This was increased to 30 mg/day over 3 weeks, with marked reduction in her symptoms. However, at the end of the 4th week of buspirone treatment she became hypomanic, exhibiting elevated mood, pressured speech, and flight of ideas. Buspirone was discontinued, and the hypomania responded to two 5-mg doses of haloperidol. Unfortunately, the patient rapidly switched into a depression with psychotic features and required hospitalization. During the ensuing 6 months, she experienced two recurrences of hypomania, which again cycled to depression with psychotic features. She has since remained euthymic on a regimen of doxepin and carbamazepine.

The exact mechanism by which buspirone exerts its anxiolytic properties is unknown, but it appears to be independent of the benzodiazepine/γ-aminobutyric acid receptors. Buspirone has been shown to bind to presynaptic dopamine receptors as well as serotonin (5-HT) receptors. Its action seems to be that of a presynaptic dopamine agonist and a 5-HT$_{1A}$ agonist; however, neither of these actions appears to explain its anxiolytic effect. Eison and Temple found that buspirone inhibits spontaneous firing of serotonergic dorsal raphe neurons (4), while spontaneous firing rates of noradrenergic cells in the locus ceruleus (concomitantly increasing levels of 3-methoxy-4-hydroxyphenylglycol sulfate, a metabolite of norepinephrine) and of dopaminergic cells in the midbrain are dramatically increased (5).

Buspirone enhances CNS catecholaminergic activity while inhibiting CNS serotonergic cell activity. CNS serotonergic and catecholaminergic systems are both hypothesized to be involved in the etiology of affective disorders. Thus, the net enhancement of noradrenergic activity relative to serotonergic activity is consistent with current hypotheses regarding the neurobiology of mania. It is noteworthy that the development of mania in this patient followed a time course similar to that observed for the onset of antidepressant efficacy.

Although this patient's manic episode could have been unrelated to buspirone, some connection is likely, since she had been monitored closely, was taking no other medication at the time, and had been medication free for 2 years prior to the onset of mania. In summary, buspirone, although marketed as an anxiolytic agent, could behave as an antidepressant, just as tricyclic antidepressants have been shown to have anxiolytic effects. It would be prudent to watch for similar effects in patients taking this class of anxiolytic drug.

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## Etiology of Somatization Disorder

SIR: The article by James Morrison, M.D., on sexual histories of women with somatization disorder (1) raised and explored important issues about the antecedents of this disorder. Shared genes and assortative mating are two genetic factors that may play a role. I would like to amplify the discussion by asking how one might detect genetic etiologic factors.

Antisocial personality disorder is evidently as heritable as alcoholism and schizophrenia (2). Females in families of antisocial males are at greater (possibly genetic) risk for somatization disorder (3–5). Therefore, if a young female were genetically at risk for somatization disorder, she would also be at greater risk of being exposed to the psychosocial factors that Dr. Morrison described (that is, being raised in proximity to antisocial males, including her father, brothers, and other male relatives, and being abused by them).

Many of the victims in Dr. Morrison's series of subjects had been assaulted by their stepfathers and stepbrothers. There seems to be assortative mating between females who have somatization disorder and antisocial males (2). If this is so, then the mothers of daughters with genetic vulnerability to somatization disorder may select subsequent male partners (stepfathers of the patients) with antisocial personality disorder and then perhaps have antisocial sons (stepbrothers of the patients), thereby exposing their daughters again to the same adverse psychosocial factors.

Twenty-seven of the perpetrators were related by blood or marriage to the 33 abuse victims with somatization disorder in Dr. Morrison's series. Thus, the phenomena of shared genes and assortative mating would have to be considered as important potential vectors in the etiology of somatization disorder.

As Dr. Morrison has pointed out elsewhere, the most telling arguments would be made by classical twin or cross-fostering studies. Short of this, some easier experiments come to mind. One could compare the abused and nonabused biological relatives of a sample of probands with antisocial personality disorder and normal control subjects. If the incidence of somatization disorder were higher in the abused group of relatives, this would be evidence for the nurture hypothesis. If the incidence were higher than that of the normal control subjects in the nonmolested group, this would be evidence that molestation was not the only factor but that other factors, environmental or genetic, have to be considered. One could also study a sample of women who were sexually abused as children, divided into subgroups according to whether or not they have biological relatives with antisocial personality disorder. If those with positive family histories have a higher incidence of somatization disorder, this would be evidence for another environmental or genetic component. Using adopted-away daughters of persons with antisocial personality disorder would be one way to provide control for nongenetic factors. Information obtained from such studies could help decide whether effort should be put into classical twin and cross-fostering experiments.

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## Another Neuroanatomical Substrate of Panic Disorder

SIR: I read with great interest the article "A Neuroanatomical Hypothesis for Panic Disorder" by Jack M. Gorman, M.D., and associates (1). I was especially interested in the relationship between acute panic attacks and the brainstem, to which the authors gave much thought on the basis of both clinical and experimental evidence. Although the authors took somewhat into account the role of limbic discharge in the development of panic attacks, they made much of the responsibility of the brainstem for these attacks.

I would like to point out the importance of the anterior cingulate gyrus as a site responsible for panic attacks. Classical neurophysiology shows us that stimulation or ablation of the anterior cingulate gyrus in experimental animals and in humans causes most of the symptoms seen in panic patients, i.e., changes in the motility of the pyloric antrum, temperature changes, shivering, piloerection, changes in respiration accompanied by cardiovascular effects and apnea, and sweating (2). Although Uhde and Kellner (3) reported no abnormal findings on CT scans of 25 patients with panic disorder, they examined only the ventricle-brain ratio. In future CT research on panic disorder, one should focus on the interhemispheric areas corresponding to Brodmann's areas 8, 9, 24, and 32 of the cerebral cortex.

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## Alzheimer's Original Paper

SIR: The editorial entitled "The Alzheimer's Disease Imperative: The Challenge for Psychiatry" (1) drew much-needed attention to a group of patients whom psychiatrists have tended to slight. The Task Force on Alzheimer's Disease rightly stressed the need for psychiatric intervention, even though we should not forget that other medical and nonmedical specialists have a place in the treatment of Alzheimer patients as well.

The editorial made reference to Alzheimer's original paper. Since that paper is in German, and since some readers might prefer an English translation, the following publication, which contains both the original paper and an English translation, may be helpful: *Alzheimer Disease and Associated Disorders, An International Journal*, Volume 1, Number 1, 1987, pages 3–8.

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## Psychiatrists' Involvement in Lawmaking Regarding the Duty to Protect

SIR: We believe that the editorial by Pierre Gagné, M.D. (1), which commented on our analysis of statutory approaches to limiting psychiatrists' liability for their patients' violent acts (2), missed the essential rationale behind such statutes. In the United States (although perhaps not yet in Canada, where Dr. Gagné practices), the principle that psychiatrists may be liable for violence committed by outpatients has spread rapidly from state to state since the decisions in *Tarasoff v. Regents of the University of California* in the mid-1970s (3). The resulting obligations have expanded psychiatrists' responsibilities well beyond traditional standards of care, extending them, for example, to control of patients' behavior months after the patients' last contacts with the psychiatric system. The duty to protect potential victims has become so much of a given that even in states without explicit rulings on the issue, psychiatrists behave (prudently, in our view) with the expectation that courts will find such a duty when the opportunity is presented.

Dr. Gagné objects to statutes defining the extent of a duty to protect third parties as "an intrusion of law into one of the most sacred territories of medicine." However, for better or worse, the law is already here; the cases defining a duty to protect potential victims create binding law as effectively as do statutes. Psychiatrists are faced with the option of abiding by an overly broad set of court-made legal rules that may have serious, deleterious effects on psychiatric practice or of helping to shape those rules through the legislative process. The latter holds out the hope of attaining a reasonable balance between the public's interest in safety and its interest in maintaining a workable context in which psychiatric treatment can take place.

Because Dr. Gagné so profoundly misunderstands the current legal situation, he also misconstrues the legal effect of the legislative solution proposed in the APA resource document, which offers a model for legislation in this area. If the proposed legislation were enacted, clinicians would be certain, for the first time, of when they have a duty to act. In addition, they would be permitted, although not legally obligated, to take protective action under threatening circumstances other than those mentioned in the APA model. Finally, clinicians would be assured that they have discharged the duty to protect by taking any one of the specified courses of action; at present, clinicians in many states do not know whether what appears to be an ethically satisfactory response will be regarded as legally satisfactory.

Dr. Gagné recognizes that the proposed model statute would reduce "the level of [professional] anxiety by clarifying the issue and limiting the conditions under which psychiatrists can be held liable." He seems to believe, however, that the proposed legislation carries too high a price. We believe, to the contrary, that if the proposed legislative solution is properly understood, considerable gains in clarity can be achieved in a way that is fully compatible with ethical standards and sound clinical practice.

The issue, from our perspective, is straightforward. Should psychiatry, in the guise of holding itself aloof from the legal process, allow the courts to determine the rules governing our liability? Or should we utilize statutory means to fashion a creative compromise that better protects the treatment interests of our patients? We favor the latter approach.

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## Dr. Gagné Replies

SIR: Dr. Appelbaum and his colleagues have reached the conclusion that I profoundly misunderstand the current legal situation regarding psychiatrists' duty to protect potential victims of their patients' violent acts. Although that remains a possibility, I must say that many colleagues, American and Canadian, who contacted me after the publication of Dr. Appelbaum and associates' article and my editorial share my concerns in regard to the influence of laws and statutes on the practice of psychiatry.

As I tried to stress in the editorial, laws do not make a patient feel better. Over the past 30 years, there has been a general feeling that more and more restrictions have been imposed on psychiatrists when it comes to determining the best approach to use in a given clinical situation. We were told that we were abusing our powers by admitting people to the hospital against their will and giving them treatment that they did not want. We have adjusted, and in many parts of the world, psychiatrists have been very involved in the writing of laws pertaining to the protection of the mentally ill.

The question I raised in the editorial is simply, Whom are we really pretending to help by becoming participants in lawmaking? My concern is that every time we do so, we are placing ourselves in a cage where, as physicians, we will be harder to reach but where, also, it will become more difficult for us to reach out and help our patients.

If my disagreement with Dr. Appelbaum and his associates is interpreted as a profound misunderstanding, I am sorry, but I am glad to disagree.

PIERRE GAGNÉ, M.D., F.R.C.P.(C)
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## Possibility of Depression as a Side Effect of Methyldopa

SIR: The first case described by Daniel J. Luchins, M.D., and Robert P. Rose, M.D., Ph.D., in their report on late-life onset of panic disorder with agoraphobia (1) indicated that the 75-year-old female patient had a history of waking at night two to three times a week with anxiety which prevented her from returning to sleep. Later on she had to restrict her activities and required the presence of another individual at all times. She had no previous psychiatric history, but it was known that she was taking a methyldopa-thiazide combination for hypertension. However, the authors did not indicate how long the patient had been taking this antihypertension medication before her visit to the psychiatric clinic. Apparently, the working diagnosis was agoraphobia, although the patient responded to desipramine, up to 75 mg/day.

It is well-known that methyldopa has been shown to reduce the tissue concentration of serotonin, dopamine, and especially norepinephrine and epinephrine (*Physicians' Desk Reference*), so it is possible that the agoraphobia and the frequent nocturnal agitation were symptoms of depression secondary to the methyldopa. The appropriate treatment plan would have been to discontinue the methyldopa first, in consultation with the patient's physician, and to substitute some other antihypertensive, such as enalapril or verapamil, which does not interfere with any neurotransmitter. Thus, one could have avoided subjecting this elderly patient to another potent medication (desipramine) and useless psychotherapy.

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## Drs. Luchins and Rose Reply

SIR: Dr. Tchen questions whether the 75-year-old patient with panic attacks and agoraphobia that we described might have been suffering from depression secondary to methyldopa. If this were the case, our treatment with desipramine and psychotherapy would have been unnecessary, since discontinuation of the offending agent would have sufficed. We do not believe the available evidence supports this viewpoint. Except for a sleep disturbance associated with nocturnal panic attacks, the patient did not have prominent depressive symptoms. She did not meet the *DSM-III-R* criteria for major depression but did meet those for panic disorder with agoraphobia. In addition, she had been taking a methyldopa-thiazide combination for several years.

More important, the relationship between methyldopa and depression is not clear-cut. The only evidence supporting such a relationship is the statement in the *Physicians' Desk Reference* that the drug reduces tissue levels of various biogenic amines. However, it has been pointed out that methyldopa does not reduce *brain* levels of catecholamines (1). Furthermore, an extensive review of clinical studies by DeMuth and Ackerman (2) provided only minimal support for the idea that depression is a consequence of methyldopa administration. First, they noted that in 16 clinical trials of methyldopa including 960 patients, only 3% were reported to show depressive symptoms, and none were judged by the reviewers to meet the *DSM-III* criteria for major depression. Second, in five studies surveying the prevalence of depression in patients treated with antihypertensive agents, the rate of depression in those taking methyldopa was not higher than in those taking other antihypertensives or in control subjects not treated with antihypertensives. Third, they could find in the English literature only three clinical reports, with a total of seven cases, of depression in individuals being treated with methyldopa. On the basis of this evidence they concluded that methyldopa is probably not "a sufficient cause of depression and that its use does not affect the prevalence of depression." Although this is perhaps too strong a conclusion, it probably is true that methyldopa, like reserpine, primarily induces depression in individuals predisposed by previous or family histories of depression (3), neither of which was the case in the patient we described.

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## Use of Benzodiazepines by Alcoholics

SIR: The comments by William J. Annitto, M.D. (1) regarding his concern about the use of benzodiazepines in alcoholics underscore an extremely important clinical dilemma for the practicing psychiatrist that has not yet been addressed. He wrote about the need for "nonaddictive" medications and receptor antagonists in prospective trials for helping recovering addicts, including alcoholics. One point which Dr. Annitto failed to mention is that the literature strongly supports the hypothesis that a substantial proportion of patients who are hospitalized for alcoholism suffer from anxiety disorders. Conservative estimates suggest that 10%–15% suffer from panic disorder, and another 20%–30% suffer from social phobia (2–5). It is also clear that a substantial percentage of patients with panic disorder or social phobia do not respond to the currently available pharmacological agents which do not produce physical dependence (e.g., antidepressants or buspirone) and are incompletely helped by behavioral treatments. In short, a substantial subgroup of patients with anxiety disorders who become alcoholic are unable to participate in the very treatment that has been shown to help them most, Alcoholics Anonymous. It seems ironic that we should deny these patients potentially helpful treatment until it has been demonstrated that this is a dangerous practice. An article by Ciraulo et al. (6) made this point very well. My colleagues' and my clinical experience in treating over 100 panic disorder patients with benzodiazepines, approximately 20% of whom had abused alcohol in the past as a direct result of their anxiety disorder, was that only two of them used the benzodiazepines in a nonmedical fashion which required discontinuation of this treatment. What the field needs at this point is a prospective, well-controlled study of alcoholics with panic disorder that investigates a variety of therapeutic techniques, including benzodiazepines. Until such studies have been completed, we should not exclude therapeutic options—we should never say never.

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## Drs. Annitto and Dackis Reply

SIR: Dr. Lydiard says never say never. We disagree. In particular, physicians should never do more harm than good for their patients.

Dr. Lydiard states that 10%–15% of alcoholics suffer from panic disorder and 20%–30% suffer from social phobia. He then implies that a substantial proportion of these patients respond only to benzodiazepines. This point is unreferenced, incorrect, and entirely misleading. Social phobia is quite responsive to β blockers (1), and panic disorder responds well to antidepressants (2, 3).

To imply that withholding benzodiazepines prevents alcoholics from participating in Alcoholics Anonymous (AA) is an example of absurd and flawed reasoning. The image of an alcoholic dosed up on benzodiazepines in an AA meeting is ridiculous to any practitioner who understands alcoholism and recovery. In an AA meeting this alcoholic would have to conceal his benzodiazepine use or be confronted with the fact that he has already relapsed to chemical dependency. Doctor, do no harm! Dr. Lydiard, read AA's "Big Book" before addicting more alcoholics to benzodiazepines.

As Dr. Lydiard states, the field needs prospective, well-controlled studies. We do not need vague descriptions of 100 patients who never admitted using benzodiazepines in a "nonmedical fashion." Indeed, before studying benzodiazepine addiction in alcoholics, it might be more pertinent to investigate benzodiazepine addiction in nonalcoholics. We predict that the results of such a study would create more anxiety in the multi-billion-dollar pharmaceutical industry than exists in the patient group studied!

We have detoxified thousands of hospitalized alcoholics over the past 10 years. Many were addicted to benzodiazepines by physicians who reasoned as Dr. Lydiard does. When will we finally consider benzodiazepine maintenance to be contraindicated in alcoholics? When will we start saying never?

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## More Comments on Patient-Therapist Sex

SIR: As psychotherapists who have treated and studied large numbers of women who are incest survivors and/or victims of sexual abuse by their therapists or others, we take strong exception to the basic tenor as well as many of the specific points raised in the article on patient-therapist sex by Thomas G. Gutheil, M.D. (1).

Although Dr. Gutheil asserted that he was not "blaming the victim," it is difficult to read his article without a strong sense that the patient's, not the therapist's, problems give rise to sexual exploitation by the therapist. The arguments that "borderline rage" "traps" therapists into "inappropriate degrees of social interaction" or that the patient's "waif-like demeanor," "boundary-blurring interpersonal manner," "manipulative skills," and "narcissistic entitlement" lead therapists astray certainly suggest it is the patient's rather than the therapist's behavior and dynamics that bear scrutiny in cases of therapist exploitation of patients. To say that these often previously abused women patients "seduce, provoke, or invite therapists into boundary violations" does not seem far from the kind of vilification we see of rape victims for behaving in a way that provokes attack or of sexually abused children for being seductive.

We are appalled at the implications of this article; there is a history in the field of psychiatry of this kind of verbal and diagnostic abuse of women patients, beginning with labeling patients' early attempts to speak of sexual misconduct by therapists as "psychotic transference" and including Freud's suggestion that hysterical patients imagined incidents of incest.

Dr. Gutheil paid no attention to the dimension of power in the therapy relationship. He did not reference current works on violence against women or current research on posttraumatic stress disorder. Since he suggested that many of these revictimized patients are survivors of earlier abuse, he would be well-advised to pay attention to this body of literature. He might think more about the difficulty these women have in protecting themselves from revictimization and less about how they "provoke" such abuse.

The implication that patients who are sexually abused by therapists have a borderline diagnosis also should be examined; it is not our experience that this is true. Furthermore, crucial questions about the borderline diagnosis are currently being raised, given the high prevalence of sexual abuse survivors who are thus diagnosed. Also, as this diagnosis is now used, it carries pejorative connotations that are broadly represented in Dr. Gutheil's article.

We are gravely concerned that many courageous women who have been abused by therapists, women who are struggling with shame and guilt and who are just now beginning to find a way to voice their complaints, will be further victimized and silenced by the kind of bias represented in this article. While Dr. Gutheil is concerned about false accusations by patients against therapists (false positives, as it were), we wish we could find in the article the same degree of concern about the many abused patients who have been shamed into silence by the judgmental attitudes of the psychiatric profession and society at large—attitudes which his article powerfully reinforces although denying responsibility for such bias. As therapists it is incumbent upon us to avoid any and all forms of victim blaming and to monitor ourselves and our colleagues so that patients can enter therapy safely, free of fears that the attempt at solution may in fact only augment the problem. To invite patients into the emotional intensity and vulnerability of psychotherapy and then violate them with either sexual exploitation or arrogant judgment is unconscionable.

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## Dr. Gutheil Replies

SIR: As a teacher who takes his teaching seriously, I become depressed whenever even one student in my class fails to get the point I am driving at. Imagine my disheartenment when five mental health professional colleagues of mine not only miss my point utterly but portray my educational effort as being itself an example of the very victimization I described (and explicitly deplored)—indeed, as being an example of a long and malignant historical tradition of victimization.

I am especially pained that in not one syllable of the letter do the authors acknowledge that my article was transparently an instruction on abuse *prevention*; nor do they seem at all aware that I described real problems deriving from real cases and offered real solutions, which have a record of helping many vulnerable, confused, or uninformed clinicians refrain from violating boundaries.

For reasons I cannot fathom, these authors write as though treatment of patients did not occur in an interactive dyad where the two parties influence each other. They imply that to study the abused patient's part of the dyad at all is somehow to begin the process of exonerating the doctor (despite my several explicit caveats against this incorrect interpretation). Can Dr. Jordan and her associates accept the complex possibility that the clinicians I described committed ethical and legal violations, malpractice, breaches of the fiduciary relationship, and abuses of a power asymmetry *and* that the patients played some role in this—a role that can be studied without shifting the slightest culpability from the doctor?

One might conclude from the letter that this topic is too "hot" even to discuss at present, what with its themes of sex, abuse, and emotions running riot. But alas, other approaches to stemming the appalling epidemic of sexual misconduct have not worked so well that my educational efforts are superfluous and redundant. How would Dr. Jordan and associates teach trainees and colleagues to avoid these tragically common pitfalls without mentioning the patients' diagnoses or symptoms, lest that seem blaming? How would they explain to the new practitioner the problems specific to the narrow population I described without mentioning the patient, lest that seem politically incorrect? Can they put aside their outrage long enough even to consider that if the educational effect of my article keeps even one fragile, insecure, ignorant, or disturbed clinician from abusing a patient, the piece has justified its publication?

THOMAS G. GUTHEIL, M.D.
*Boston, Mass.*

## Treatment of Depression in Patients With Dementia

SIR: I find that I must take exception to the suggestion by Dilip Ramchandani, M.D. (1) that biologic treatment of depression in patients with irreversible dementia or pseudodementia may "hasten the course of dementia." There are, as far as I know, no data to support the statement that antidepressants and ECT affect the prognosis of a dementing disorder. Indeed, vigorous treatment of depressive symptoms usually improves cognitive dysfunction and quality of life even though an underlying dementia may not be affected. To suggest that effective treatment be withheld on the basis of unsupported speculation is clearly unwarranted.

Kral and Emery's interesting work on the long-term prognosis of depressive pseudodementia (2) did not address the issue of treatment effects. Even if depressive pseudodementia eventually progresses to an irreversible dementia, this does not obviate the need to treat the depressive illness early in its course. Certainly, patients may return to a higher level of functioning than if their dementia is further complicated by significant depressive symptoms. Rovner et al. (3) suggested that anticholinergic side effects of tricyclic antidepressants may worsen cognitive functioning in the elderly, but there are antidepressants available that have minimal anticholinergic activity (4). Until more effective treatments are clearly demonstrated, antidepressants and ECT should be considered in treating depressive pseudodementia or a mixed depression and dementia syndrome.

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### Dr. Ramchandani Replies

SIR: Dr. Lam's objection appears to stem from the perspective that depression and dementia are distinct illnesses, which indeed they can be. My letter was an attempt, primarily, to focus on the overlap between these two conditions and, secondarily, to caution about overtreatment. I have no quarrel with the notion of a considered trial of antidepressants or ECT in such patients. It can, however, be argued that the sparseness of data supporting the noxious effects of tricyclics or ECT (1–3) in dementing disorders is more a reflection of sparse investigation (4) than a negation of the possibility of these effects.

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DILIP RAMCHANDANI, M.D.
*Philadelphia, Pa.*

### Effect of Medication on Patients' Neuropsychological Functioning

SIR: The article "Neurological Impairment in Violent Schizophrenic Inpatients" by Menahem I. Krakowski, M.D., Ph.D., and associates (1) was a careful comparison of neurological and neuropsychological studies on a therapeutically difficult category of patients. In view of the difficulties in management, violent patients are likely to be more heavily medicated with neuroleptic drugs than nonviolent patients who have comparable diagnoses. It would therefore have been important to have data on whether the nonviolent control patients were given less psychotropic medication than the violent patients.

Some of the effects of heavy and/or chronic medication with neuroleptics could have affected such parameters as hopping, walking-associated movements, pronation-supination, tandem walk, and possibly others of the neurological signs observed. Similarly, mental function, as measured by tests for organicity (table 2 in the article), could have been affected by neuroleptic drugs, especially those with sedative properties. Other medications that might be given to violent patients, such as anxiolytic or sedative drugs, could have impaired the patients' performance on some of the parameters studied.

Since the authors were careful to consider drug or alcohol abuse and presumably eliminated this variable, it seems likely that they also considered medication. A statement to the effect that psychotropic medication was, was not, or could have been a variable would be helpful.

REFERENCE

1. Krakowski MI, Convit A, Jaeger J, et al: Neurological impairment in violent schizophrenic inpatients. Am J Psychiatry 1989; 146:849–853

LUCAS S. VAN ORDEN, M.D., PH.D.
*Iowa City, Iowa*

### Dr. Krakowski and Associates Reply

SIR: Dr. Van Orden correctly points out the importance of considering the contribution of neuroleptic medications to neurological and neuropsychological impairment. The effect of various medications was investigated. There were no differences in doses of neuroleptics, lithium, or anxiolytic medications among the high violence, low violence, and control patients. In addition to comparing doses among the three groups, we also entered dose of neuroleptic medication (in chlorpromazine equivalents) as a covariate in analyses of covariance, to control for the possible confounding effects of medication on neurological and neuropsychological assessments. The differences among groups remained highly significant, whereas the covariate effects were not significant. The analysis of covariance for the neurological impairment score ($F=10.1$, $df=2, 80$, $p<0.001$) was reported in the article on page 851; the covariate effect was not significant ($F=0.05$, $p=0.83$).

MENAHEM I. KRAKOWSKI, M.D., PH.D.
ANTONIO CONVIT, M.D.
JUDITH JAEGER, PH.D.
SHANG LIN, PH.D.
JAN VOLAVKA, M.D., PH.D.
*Orangeburg, N.Y.*

### Categorization of Housewives as Unskilled/Unemployed

SIR: In her article "Physical and Sexual Assault Histories Among Psychiatric Outpatients" (1), Andrea Jacobson, M.D., Ph.D., performed an insidious disservice to many women when she categorized one group of study patients as "unskilled/unemployed individuals (including housewives)." It is possible that all the housewives in Dr. Jacobson's study were unskilled, "unemployed"—which in this context would mean currently being unmarried!—or both. It is far more likely, however, that these women were occupied as full-time homemakers, performing the multiple tasks that this job entails with varying levels of skill. It is also likely that Dr. Jacobson's grouping of these women together with those who were truly unskilled or unemployed reflects the author's own attitude toward women who choose to make careers of being wives, mothers, and homemakers. This is an attitude held by many in our society, but it has no place in the pages of this journal or in the minds of psychiatrists who treat women.

Therefore, I propose that homemakers be given their own category in future studies to be published in the *Journal*. This will more accurately reflect these subjects' priorities and their occupations while not belittling either their skills or their accomplishments.

REFERENCE

1. Jacobson A: Physical and sexual assault histories among psychiatric outpatients. Am J Psychiatry 1989; 146:755–758

LYNN S. BAKER, M.D.
*Santa Monica, Calif.*

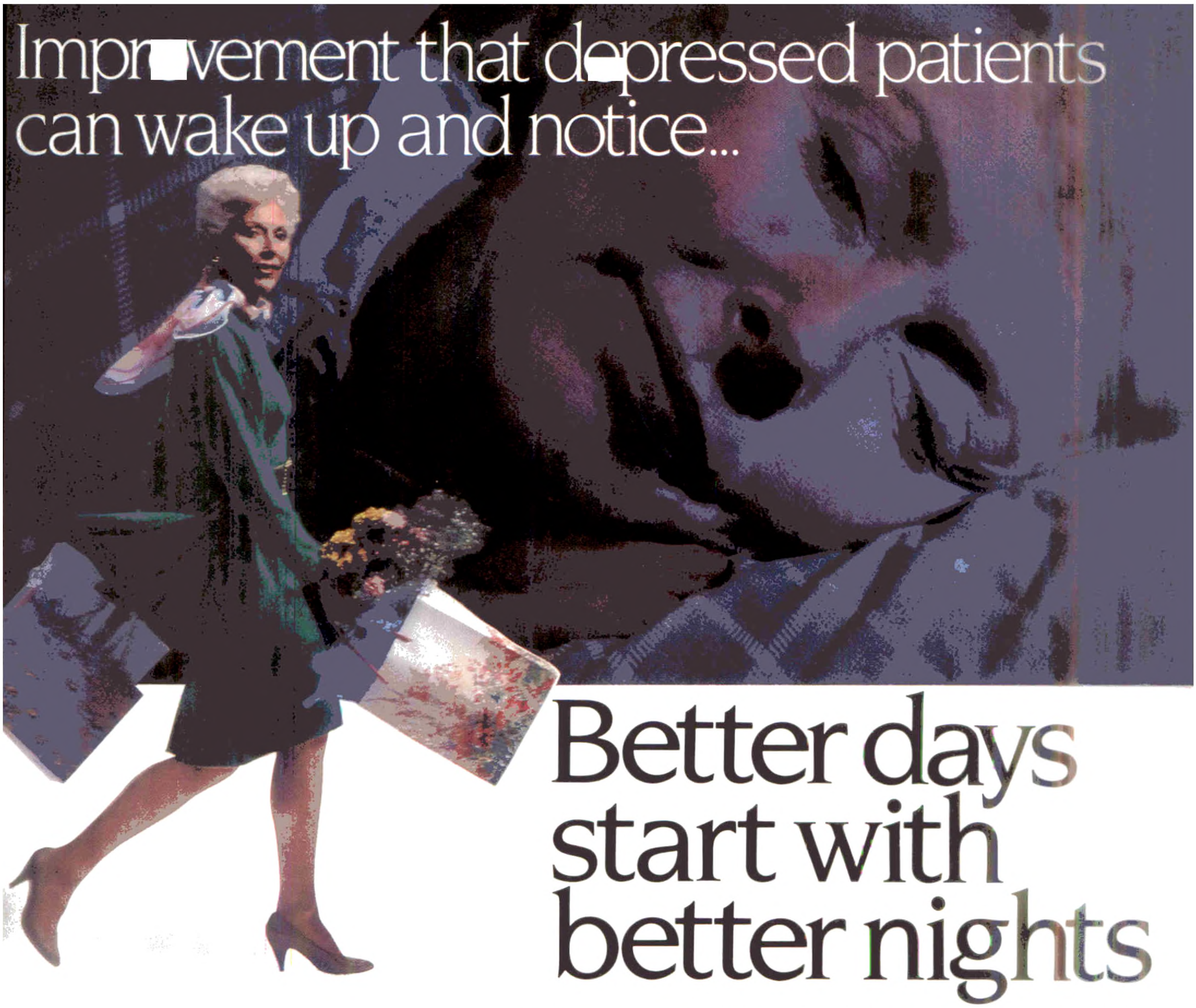
**Dr. Jacobson Replies**

SIR: Dr. Baker is absolutely right in her criticism of the category "unskilled/unemployed individuals (including housewives)." I am appalled that I did not notice this and appreciate her pointing it out. The phrase comes from an old and often-used method of describing socioeconomic status (Hollingshead-Redlich), and I included it mindlessly on a demographic sheet used by interviewers. Patients were not exposed to the phrase, and in calculating socioeconomic status we did not use the category for housewives. But the error serves to remind all of us of the need to scrutinize established tests and procedures for sexist content.

My error in using the old categorization of housewives does not, as Dr. Baker seems to assume, reflect my own attitude toward homemakers. In my clinical practice I ask patients whether they work in the home, outside the home, or both. This question is well-received by homemakers. In the ongoing process of examining our work for sexism, we would all do well to be patient with one another and not assume the worst.

ANDREA JACOBSON, M.D., PH.D.
*Seattle, Wash.*

*Reprints of letters to the Editor are not available.*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*Please see brief summary of SINEQUAN® (doxepin HCl) prescribing information on next page.*

ROERIG Pfizer
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**References: 1.** Goldberg HL: Sleep disturbance as a manifestation of depression, in *Somatic Depression: Insights for Primary Care Physicians*. Proceedings of a symposium held in Miami, Dec 4, 1978. New York, Postgraduate Medicine Communications, pp 13-18. **2.** Karacan I, Blackburn AB, Thornby JI, et al: The effect of doxepin HCl (Sinequan) on sleep patterns and clinical symptomatology of neurotic depressed patients with sleep disturbance, in *Sinequan® (doxepin HCl): A Monograph of Recent Clinical Studies*. Princeton, NJ, Excerpta Medica, 1977, pp 4-22. **3.** Goldberg HL, Finnerty RJ: The use of doxepin in the treatment of symptoms of anxiety neurosis and accompanying depression: A collaborative controlled study. *Am J Psychiatry* 1972;129(July):74-77.

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# SINEQUAN® (doxepin HCl)

**BRIEF SUMMARY**
**SINEQUAN® (doxepin HCl) Capsules/Oral Concentrate**

**Contraindications.** SINEQUAN is contraindicated in individuals who have shown hypersensitivity to the drug. Possibility of cross sensitivity with other dibenzoxepines should be kept in mind.

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**Warnings.** The once-a-day dosage regimen of SINEQUAN in patients with intercurrent illness or patients taking other medications should be carefully adjusted. This is especially important in patients receiving other medications with anticholinergic effects.

***Usage in Geriatrics:*** The use of SINEQUAN on a once-a-day dosage regimen in geriatric patients should be adjusted carefully based on the patient's condition.

***Usage in Pregnancy:*** Reproduction studies have been performed in rats, rabbits, monkeys and dogs and there was no evidence of harm to the animal fetus. The relevance to humans is not known. Since there is no experience in pregnant women who have received this drug, safety in pregnancy has not been established. There has been a report of apnea and drowsiness occurring in a nursing infant whose mother was taking SINEQUAN.

***Usage in Children:*** The use of SINEQUAN in children under 12 years of age is not recommended because safe conditions for its use have not been established.

**Drug Interactions.**

***MAO Inhibitors:*** Serious side effects and even death have been reported following the concomitant use of certain drugs with MAO inhibitors. Therefore, MAO inhibitors should be discontinued at least two weeks prior to the cautious initiation of therapy with SINEQUAN. The exact length of time may vary and is dependent upon the particular MAO inhibitor being used, the length of time it has been administered, and the dosage involved.

***Cimetidine:*** Cimetidine has been reported to produce clinically significant fluctuations in steady-state serum concentrations of various tricyclic antidepressants. Serious anticholinergic symptoms (i.e., severe dry mouth, urinary retention and blurred vision) have been associated with elevations in the serum levels of tricyclic antidepressant when cimetidine therapy is initiated. Additionally, higher than expected tricyclic antidepressant levels have been observed when they are begun in patients already taking cimetidine. In patients who have been reported to be well controlled on tricyclic antidepressants receiving concurrent cimetidine therapy, discontinuation of cimetidine has been reported to decrease established steady-state serum tricyclic antidepressant levels and compromise their therapeutic effects.

***Alcohol:*** It should be borne in mind that alcohol ingestion may increase the danger inherent in any intentional or unintentional SINEQUAN overdosage. This is especially important in patients who may use alcohol excessively.

***Tolazamide:*** A case of severe hypoglycemia has been reported in a type II diabetic patient maintained on tolazamide (1 gm/day) 11 days after the addition of doxepin (75 mg/day).

**Precautions.** Since drowsiness may occur with the use of this drug, patients should be warned of the possibility and cautioned against driving a car or operating dangerous machinery while taking the drug. Patients should also be cautioned that their response to alcohol may be potentiated.

Since suicide is an inherent risk in any depressed patient and may remain so until significant improvement has occurred, patients should be closely supervised during the early course of therapy. Prescriptions should be written for the smallest feasible amount.

Should increased symptoms of psychosis or shift to manic symptomatology occur, it may be necessary to reduce dosage or add a major tranquilizer to the dosage regimen.

**Adverse Reactions. NOTE:** Some of the adverse reactions noted below have not been specifically reported with SINEQUAN use. However, due to the close pharmacological similarities among the tricyclics, the reactions should be considered when prescribing SINEQUAN (doxepin HCl).

*Anticholinergic Effects:* Dry mouth, blurred vision, constipation, and urinary retention have been reported. If they do not subside with continued therapy, or become severe, it may be necessary to reduce the dosage.

*Central Nervous System Effects:* Drowsiness is the most commonly noticed side effect. This tends to disappear as therapy is continued. Other infrequently reported CNS side effects are confusion, disorientation, hallucinations, numbness, paresthesias, ataxia, extrapyramidal symptoms, seizures, tardive dyskinesia, and tremor.

*Cardiovascular:* Cardiovascular effects including hypotension, hypertension, and tachycardia have been reported occasionally.

*Allergic:* Skin rash, edema, photosensitization, and pruritus have occasionally occurred.

*Hematologic:* Eosinophilia has been reported in a few patients. There have been occasional reports of bone marrow depression manifesting as agranulocytosis, leukopenia, thrombocytopenia, and purpura.

*Gastrointestinal:* Nausea, vomiting, indigestion, taste disturbances, diarrhea, anorexia, and aphthous stomatitis have been reported. (See anticholinergic effects.)

*Endocrine:* Raised or lowered libido, testicular swelling, gynecomastia in males, enlargement of breasts and galactorrhea in the female, raising or lowering of blood sugar levels, and syndrome of inappropriate antidiuretic hormone secretion have been reported with tricyclic administration.

*Other:* Dizziness, tinnitus, weight gain, sweating, chills, fatigue, weakness, flushing, jaundice, alopecia, headache, exacerbation of asthma, and hyperpyrexia (in association with chlorpromazine) have been occasionally observed as adverse effects.

*Withdrawal Symptoms:* The possibility of development of withdrawal symptoms upon abrupt cessation of treatment after prolonged SINEQUAN administration should be borne in mind. These are not indicative of addiction and gradual withdrawal of medication should not cause these symptoms.

**Dosage and Administration.** For most patients with illness of mild to moderate severity, a starting daily dose of 75 mg is recommended. Dosage may subsequently be increased or decreased at appropriate intervals and according to individual response. The usual optimum dose range is 75 mg/day to 150 mg/day.

In more severely ill patients higher doses may be required with subsequent gradual increase to 300 mg/day if necessary. Additional therapeutic effect is rarely to be obtained by exceeding a dose of 300 mg/day.

In patients with very mild symptomatology or emotional symptoms accompanying organic disease, lower doses may suffice. Some of these patients have been controlled on doses as low as 25-50 mg/day.

The total daily dosage of SINEQUAN may be given on a divided or once-a-day dosage schedule. If the once-a-day schedule is employed the maximum recommended dose is 150 mg/day. This dose may be given at bedtime. **The 150 mg capsule strength is intended for maintenance therapy only and is not recommended for initiation of treatment.**

Anti-anxiety effect is apparent before the antidepressant effect. Optimal antidepressant effect may not be evident for two to three weeks.

**Overdosage.**

A. Signs and Symptoms

1. Mild: Drowsiness, stupor, blurred vision, excessive dryness of mouth.
2. Severe: Respiratory depression, hypotension, coma, convulsions, cardiac arrhythmias and tachycardias.

Also: urinary retention (bladder atony), decreased gastrointestinal motility (paralytic ileus), hyperthermia (or hypothermia), hypertension, dilated pupils, hyperactive reflexes.

B. Management and Treatment

1. Mild: Observation and supportive therapy is all that is usually necessary.
2. Severe: Medical management of severe SINEQUAN overdosage consists of aggressive supportive therapy. If the patient is conscious, gastric lavage, with appropriate precautions to prevent pulmonary aspiration, should be performed even though SINEQUAN is rapidly absorbed. The use of activated charcoal has been recommended, as has been continuous gastric lavage with saline for 24 hours or more. An adequate airway should be established in comatose patients and assisted ventilation used if necessary. EKG monitoring may be required for several days, since relapse after apparent recovery has been reported. Arrhythmias should be treated with the appropriate antiarrhythmic agent. It has been reported that many of the cardiovascular and CNS symptoms of tricyclic antidepressant poisoning in adults may be reversed by the slow intravenous administration of 1 mg to 3 mg of physostigmine salicylate. Because physostigmine is rapidly metabolized, the dosage should be repeated as required. Convulsions may respond to standard anticonvulsant therapy, however, barbiturates may potentiate any respiratory depression. Dialysis and forced diuresis generally are not of value in the management of overdosage due to high tissue and protein binding of SINEQUAN.

**More detailed professional information available on request.**

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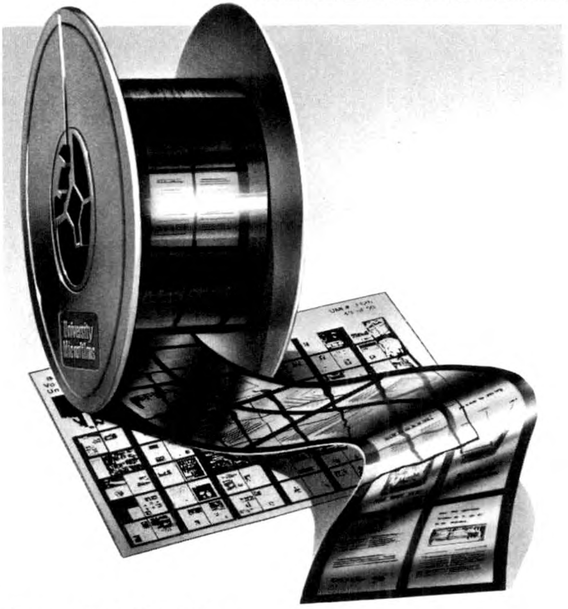

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# THORAZINE®

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**See adjacent page for brief summary of prescribing information.**

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**See complete prescribing information in SK&F literature or *PDR*. The following is a brief summary.**

**Contraindications:** Comatose states or presence of large amounts of C.N.S. depressants.

**Warnings: The possibility of extrapyramidal reactions from chlorpromazine may confuse the diagnosis of Reye's syndrome or other encephalopathy. Therefore, avoid use in children or adolescents with suspected Reye's syndrome.**

May cause persistent tardive dyskinesia, which appears to be irreversible in some patients. Reserve chronic neuroleptic treatment for patients with chronic illness 1) that is known to respond to neuroleptics and 2) for whom there are no safer but equally effective treatment options. Use the smallest effective dose over the shortest treatment duration. If signs and symptoms of tardive dyskinesia develop, consider discontinuing the neuroleptic. A potentially fatal symptom complex sometimes referred to as Neuroleptic Malignant Syndrome (NMS) has been reported in association with antipsychotic drugs. To manage NMS 1) discontinue immediately antipsychotic drugs and any other drugs not essential to concurrent therapy; 2) treat symptoms intensively and monitor; 3) where possible, treat serious concomitant medical problems. If antipsychotic treatment is needed after recovery from NMS, consider reintroducing drug therapy and monitor the patient carefully as recurrences of NMS have been reported. 'Thorazine' ampuls and vials contain sodium bisulfite and sodium sulfite; the sulfite may cause allergic reactions, including anaphylactic symptoms. In patients with bone marrow depression or previously demonstrated hypersensitivity (e.g., blood dyscrasias, jaundice) with phenothiazines, do not administer 'Thorazine' unless the potential treatment benefits outweigh the possible hazards. Caution patients about activities requiring alertness (e.g., operating vehicles or machinery) especially during the first few days therapy. Avoid concomitant use with alcohol. May counteract antihypertensive effect of guanethidine and related compounds. Use in pregnancy only when essential. There are reported instances of prolonged jaundice, extrapyramidal signs, hyperreflexia or hyporeflexia in newborns whose mothers had received chlorpromazine. Chlorpromazine is excreted in the breast milk of nursing mothers.

**Precautions:** Advise patients and/or guardians of the risk of tardive dyskinesia from chronic therapy. Use cautiously in persons with cardiovascular, liver, renal or chronic respiratory disease, or with acute respiratory infections. Patients with a history of hepatic encephalopathy due to cirrhosis have increased sensitivity to the C.N.S. effects of chlorpromazine. Due to cough reflex suppression, aspiration of vomitus is possible. May prolong or intensify the action of C.N.S. depressants, organophosphorus insecticides, heat, atropine and related drugs. (Reduce dosage of concomitant C.N.S. depressants.) Anticonvulsant action of barbiturates is not intensified.

Neuroleptic drugs cause elevated prolactin levels that persist during chronic administration. Since approximately one third of human breast cancers are prolactin-dependent *in vitro*, this elevation is of potential importance if neuroleptic drug administration is contemplated in a patient with a previously detected breast cancer. Neither clinical nor epidemiologic studies to date, however, have shown an association between the chronic administration of neuroleptic drugs and mammary tumorigenesis. Chromosomal aberrations in spermatocytes and abnormal sperm have been demonstrated in rodents treated with certain neuroleptics. Use cautiously in glaucoma patients. May diminish the effect of oral anticoagulants, produce α-adrenergic blockade, and lower the convulsive threshold; dosage adjustment of anticonvulsants may be required. May interfere with Dilantin®* metabolism, causing 'Dilantin' toxicity. May cause false positive phenylketonuria test results. Do not use with Amipaque®†. Discontinue 'Thorazine' at least 48 hours before myelography, do not resume for at least 24 hours postprocedure, and do not use to control N/V prior to myelography or postprocedure with 'Amipaque'. Evaluate patients with a history of long-term therapy with 'Thorazine' and/or other neuroleptics periodically to decide whether the dosage could be reduced or therapy discontinued. Antiemetic effect may mask signs of overdosage of other drugs or obscure diagnosis and treatment of conditions such as intestinal obstruction, brain tumor and Reye's syndrome (see Warnings). When used concomitantly, may obscure vomiting as a sign of toxicity of a cancer chemotherapeutic agent. Discontinue high-dose, long-term therapy gradually. Patients with a history of long-term therapy with 'Thorazine' and/or other neuroleptics should be evaluated periodically for possible adjustment or discontinuance of drug therapy.

**Adverse Reactions:** Drowsiness; cholestatic jaundice; agranulocytosis, eosinophilia, leukopenia, hemolytic anemia, aplastic anemia, thrombocytopenic purpura and pancytopenia; postural hypotension, tachycardia, fainting, dizziness and occasionally a shock-like condition; reversal of epinephrine effects; EKG changes have been reported; neuromuscular (extrapyramidal) reactions: dystonias, motor restlessness, pseudo-parkinsonism, persistent tardive dyskinesia, psychotic symptoms, catatonic-like states, cerebral edema; convulsive seizures; abnormality of the cerebrospinal fluid proteins; urticarial reactions and photosensitivity, exfoliative dermatitis, contact dermatitis; asthma, laryngeal edema, angioneurotic edema, and anaphylactoid reactions; lactation and breast engorgement (in females on large doses), false positive pregnancy tests, amenorrhea, gynecomastia; hyperglycemia, hypoglycemia, glycosuria; dry mouth, nasal congestion, constipation, adynamic ileus, urinary retention, priapism, miosis, mydriasis; after prolonged substantial doses, skin pigmentation, epithelial keratopathy, lenticular and corneal deposits and pigmentary retinopathy, visual impairment; mild fever (after large I.M. doses); hyperpyrexia; increased appetite and weight; a systemic lupus erythematosus-like syndrome; peripheral edema.

NOTE: Sudden death in patients taking phenothiazines (apparently due to cardiac arrest or asphyxia due to failure of cough reflex) has been reported but no causal relationship has been established.

**How Supplied: Tablets:** 10 mg, 25 mg or 50 mg, in bottles of 100 and 1000; in Single Unit Packages of 100 (intended for institutional use only). For use in severe neuropsychiatric conditions, 100 mg and 200 mg, in bottles of 100 and 1000; in Single Unit Packages of 100 (intended for institutional use only).

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# Calendar

*(Continued from page A12)*

Tawan Hospital, P.O. Box 15258 Al Ain, Abu Dhabi, United Arab Emirates; 677444.

## MAY

May 3–4, International Congress on Treatment of Mental Illness and Behavioral Disorder in Mentally Retarded Persons, Amsterdam. Contact Netherlands Organization for Postacademic Education in the Social Sciences (PAOS), P.O. Box 325, 2300 AH Leiden, Netherlands; (0)71-278027.

May 12–17, 143rd Annual Meeting of the American Psychiatric Association, New York. Contact Cathy Earnest-Nash, Office to Coordinate the Annual Meeting, APA, 1400 K Street, NW, Washington, DC 20005; 202-682-6237.

May 22–24, 2nd World Congress on Chronic Rhonchopathy, Barcelona, Spain. Contact Secretaria Tecnica, BRP Barcelona Relaciones Publicas, Edificio Layetana, Calle Pau Claris, n. 138, 7o 4o, 08009 Barcelona, Spain; 93-215-7214.

May 22–25, regional symposium, World Psychiatric Association, Hong Kong. Contact Dr. C.M. Chung, 611 Melbourne Plaza, Queen's Road, Central Hong Kong, China.

May 24–25, "Day Treatment of Children," The Clarke Institute of Psychiatry, Child and Family Studies Centre, Toronto. Contact Thomas Yoannidis, Clarke Institute of Psychiatry, 250 College Street, Toronto, Ontario, M5T 1R8; 416-979-2221, ext. 2260.

May 29–June 3, 9th International Conference on Psychosomatic Obstetrics and Gynecology, Amsterdam. Contact Ms. G. van Notten, Europaplein 8, 1078 GZ Amsterdam, Netherlands.

May 31–June 2, "Psychiatric Epidemiology and Primary Health Care," organized by the World Psychiatric Association Section of Epidemiology and Community Psychiatry, Toronto. Contact Professor M.R. Eastwood, Department of Psychiatry, Clarke Institute of Psychiatry, 250 College Street, Toronto, Ontario, Canada.

## JUNE

June 3–6, annual meeting, Canadian College of Neuropsychopharmacology, Banff, Alberta. Contact Gl[illegible] Baker, Chairman, Organizing Committee, Neurochemical Research Unit, Department of Psychiatry, Mackenzie Centre, University of Alberta, Edmonton, Alberta, Canada, T6G [illegible]37; 403-492-6591.

June 6–8, 5th Congress of the International Federation of Psychiatric Epidemiology, Montreal. Contact Head Office of the Congress, 2 Complexe Desjardins East Tower, Entrance 3000, P.O. Box 216, Station Desjardins, Montreal, Quebec, Canada, H5B 1C8; 514-845-3259.

June 11–12, 4th Annual National Institute of Mental Health International Research Conference on the Classification and Treatment of Mental Disorders in General Health Care Settings, Rockville, Maryland. Contact David B. Lar[illegible]n, M.D., M.S.P.H., or Kelly H. Kelleher, M.D., M.P.H., c/o The Primary Care Research Program, Biometric and Clinical Applications Branch, Division of Biometry and Applied Sciences, National Institute of Mental Health, 5600 Fishers Lane, Room 18C-14, Rockville, MD 20857; 301-443-[illegible]3[illegible]

June 13–15, 1st International Conference on "Crisis Intervention Approach in Mental Health," Regents College, London. Contact Dr. N. Rao Punukollu, Coordinator, International Scientific Advisory Group, 63 Naber[illegible]t Lane, Crosland Moor, Huddersfield, HD4 5DJ, England; 0484-654711, ext. 3588.

June 16–19, "Neurological and Neuropsychological Complications of HIV Infection: Update 1990," a conference prior to the VI International Conference on AIDS, Monterey, California. Contact Conference Secretariat, Ker[illegible]ess Canada, Inc., P.O. Box 200, Station B, Montreal, Quebec Canada H3B 3J7; 514-874-1622.

June 24–27, 3rd Symposium on Violence and Aggression, Saskatoon, Saskatchewan. Contact Thelma How[illegible]d, Planning Committee, Division of Extension and Community Relations, University of Saskatchewan, Saskatoon, Saskatchewan, Canada S7N 0W0.

June 24–28, 6th Annual Conference on Children-in-War, Jerusalem. Contact Dr. Roberta Apfel, Program Director, Sigmund Freud Center, Hebrew University of Jerusalem, Mount Scopus, Jerusalem 91905 Israel; 02-883[illegible]

# Books Received

**Understanding Women in Distress**, by Pamela Ashurst and Zaida Hall, et al. New York, Tavistock/Routledge, 1989, 231 pp., $49.95; $14.95 (paper).

**Geriatrics Review Syllabus: A Core Curriculum in Geriatric Medicine, Book I: Syllabus and Questions, 1989–1990 Program**, edited by John C. Beck, M.D. New York, American Geriatrics Society, 1989, 332 pp., no price listed (paper).

**Child Psychiatry and the Law**, edited by Dora Black, Stephen Wolkind, and Jean Harris Hendriks. London, Gaskell (Royal College of Psychiatrists), 1989, 178 pp., £10.00 (paper).

**The Empathic Reader: A Study of the Narcissistic Character and the Drama of the Self**, by J. Brooks Bouson. Amherst, University of Massachusetts Press, 1989, 196 pp., $25.00.

**Why They Don't Call When They Say They Will and Other Mixed Signals**, by Joy Browne. New York, Simon & Schuster, 1989, 203 pp., $18.95.

**The Improbable Machine: What the Upheavals in Artificial Intelligence Research Reveal About How the Mind Really Works**, by Jeremy Campbell. New York, Simon & Schuster, 1989, 322 pp., $19.95.

**MCQ Tutor: Psychiatry Today**, by Robert I. Cohen, M.R.C.Psych., and Aideen O'Halloran, M.R.C.P. Oxford, Heinemann Medical Books, 1989, 129 pp., $29.95 (paper).

**One to One: Experiences of Psychotherapy** (1988), by Rosemary Dinnage. New York, Penguin Books, 1989, 218 pp., $8.95 (paper).

**Psychic Equilibrium and Psychic Change: Selected Papers of Betty Joseph: New Library of Psychoanalysis 9**, edited by Michael Feldman and Elizabeth Bott Spillius; David Tuckett, general editor. New York, Routledge in association with the Institute of Psychoanalysis, London, 1989, 222 pp., $45.00; $15.95 (paper).

**Research Methods in Psychiatry: A Beginner's Guide**, edited by Chris Freeman and Peter Tyrer. London, Gaskell (Royal College of Psychiatrists), 1989, 231 pp., £10.00 (paper).

**Control Your Dreams: How Lucid Dreaming Can Help You Uncover Your Hidden Desires, Confront Your Hidden Fears, and Explore the Frontiers of Human Consciousness**, by Jayne Gackenbach and Jane Bosveld. New York, Harper & Row, 1989, 226 pp., $16.95.

**What Children Can Tell Us: Eliciting, Interpreting, and Evaluating Information From Children**, by James Garbarino, Frances M. Stott, and Faculty of the Erikson Institute. San Francisco, Jossey-Bass, 1989, 353 pp., $24.95.

**Control Theory in the Practice of Reality Therapy: Case Studies**, edited by Naomi Glasser; commentary by William Glasser, M.D. New York, Perennial Library (Harper & Row), 1989, 309 pp., $8.95 (paper).

**Handbook of Psychooncology: Psychological Care of the Patient With Cancer**, edited by Jimmie C. Holland, M.D., and Julia H. Rowland, Ph.D. New York, Oxford University Press, 1989, 771 pp., $95.00.

**Users and Abusers of Psychiatry: A Critical Look at Traditional Psychiatric Practice**, by Lucy Johnstone. New York, Routledge, 1989, 304 pp., $45.00; $16.95 (paper).

**Narcissistic Personality Disorder: The Psychiatric Clinics of America, vol. 12, number 3, September 1989**, edited by O Kernberg, M.D. Philadelphia, W.B. Saunders Co. (Harcourt Jovanovich), 1989, 266 pp., no price listed.

**Animal Models of Depression**, edited by George F. Koob, Cin Ehlers, and David J. Kupfer. Boston, Birkhäuser (New Springer-Verlag, distributor), 1989, 284 pp., $55.00.

**In-Patient Treatment for Alcoholism: A Multi-Centre Evalu Study**, by Heinrich Küfner and William Feuerlein in collabor with Klaus Antons, Dieter Feidel, Thomas Flohrschütz, Hansert, and Manfred Huber. New York, Springer-Verlag, 377 pp., $88.10

**The Neuropharmacological Basis of Reward**, edited by Jeffr Liebman and Steven J. Cooper. New York, Clarendon Press ford University Press), 1989, 424 pp., $75.00.

**The Art of Counseling, revised ed.**, by Rollo May. New York, ner Press, 1989, 185 pp., $19.95.

**Testers and Testing: The Sociology of School Psychology**, by Milofsky. New Brunswick, N.J., Rutgers University Press, 261 pp., $35.00; $14.00 (paper).

**Social Causes of Psychological Distress**, by John Mirowsky Catherine E. Ross. New York, Aldine de Gruyter, 1989, 20 $31.95; $16.95 (paper).

**Boyhood Rituals in an African Society: An Interpretation**, by S Ottenberg. Seattle, University of Washington Press, 1989, pp., $30.00.

**Understanding Your Therapist, or, Why Is This Taking So Lon** Robert H. Pilpel. Chicago, Contemporary Books, 1989, 9 $6.95 (paper).

**Hispanics and Mental Health: A Framework for Research**, by H. Rogler, Robert G. Malgady, and Orlando Rodriguez. Mal Fla., Robert E. Krieger, 1989, 154 pp., $19.50.

**Seasons of the Mind: Why You Get the Winter Blues and Wha Can Do About It**, by Norman E. Rosenthal, M.D. New Bantam Books, 1989, 267 pp., $18.95.

**Sex in the Forbidden Zone: When Men in Power—Therapists, tors, Clergy, Teachers, and Others—Betray Women's Tru** Peter Rutter, M.D. Los Angeles, Jeremy P. Tarcher, 1989, 24 $17.95.

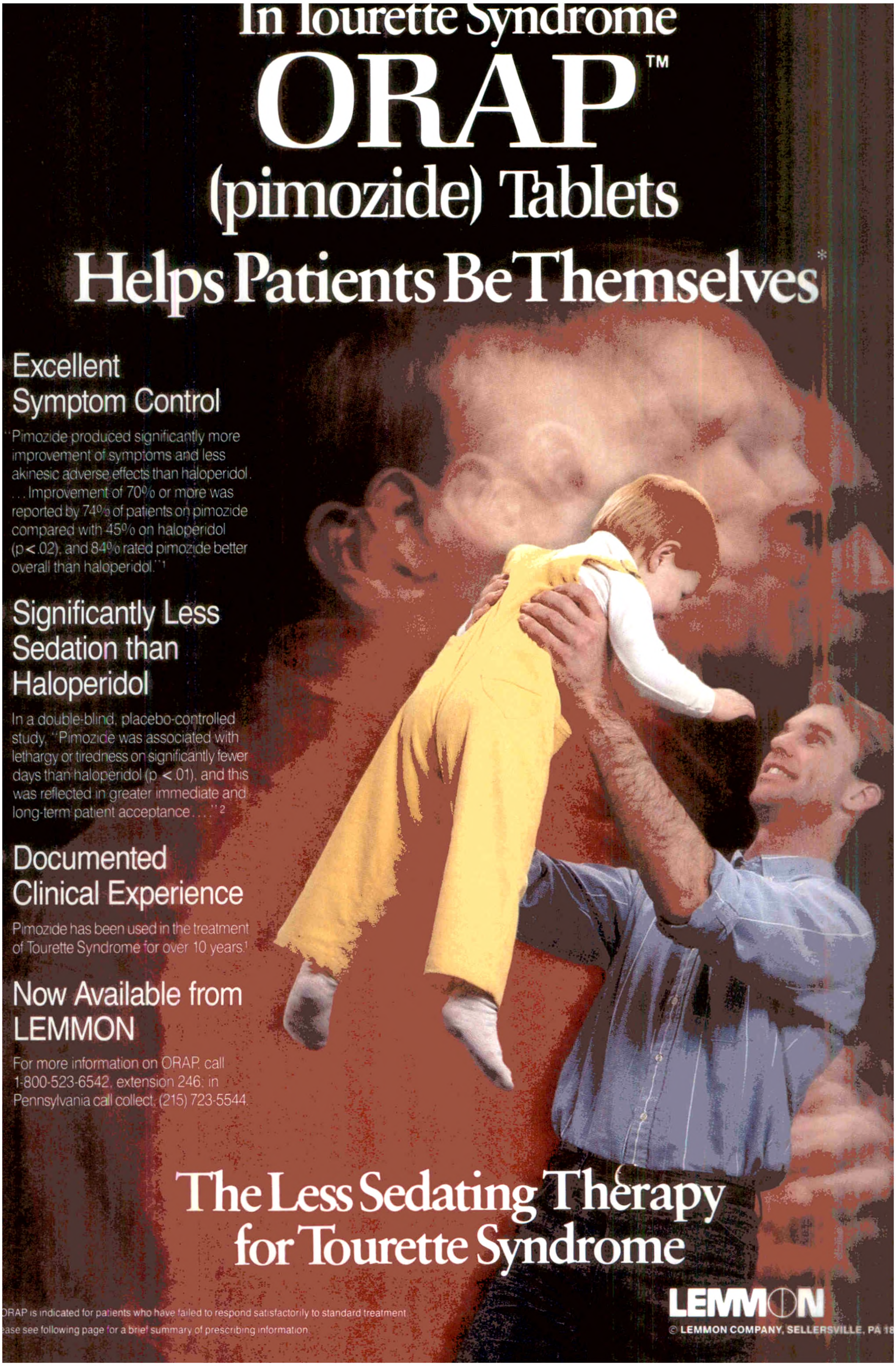
**The European Colloquium on Medical Ethics: Jewish Perspec** edited by Avraham Steinberg, M.D. Jerusalem, Magnes Press brew University, 1989, 223 pp., $14.00 (paper).

**The Psychology of Deafness: Understanding Deaf and Ha Hearing People**, by McCay Vernon and Jean F. Andrews. York, Longman, 1990, 281 pp., no price listed.

**Terrifying Love: Why Battered Women Kill and How Societ sponds**, by Lenore E. Walker. New York, Harper & Row, 336 pp., $18.95.

**The Troubled Adolescent**, by Joseph L. White. Oxford, Perg Press, 1989, 365 pp., $45.00; $19.50 (paper).

**Social Treatment: An Introduction to Interpersonal Helping i cial Work Practice, 2nd ed.**, by James K. Whittaker and Eliz M. Tracy. New York, Aldine de Gruyter, 1989, 265 pp., $3 $16.95 (paper).



# In Tourette Syndrome ORAP™ (pimozide) Tablets Helps Patients Be Themselves*

## Excellent Symptom Control

"Pimozide produced significantly more improvement of symptoms and less akinesic adverse effects than haloperidol. . . . Improvement of 70% or more was reported by 74% of patients on pimozide compared with 45% on haloperidol ($p < .02$), and 84% rated pimozide better overall than haloperidol."[1]

## Significantly Less Sedation than Haloperidol

In a double-blind, placebo-controlled study, "Pimozide was associated with lethargy or tiredness on significantly fewer days than haloperidol ($p < .01$), and this was reflected in greater immediate and long-term patient acceptance . . . ."[2]

## Documented Clinical Experience

Pimozide has been used in the treatment of Tourette Syndrome for over 10 years.[1]

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## The Less Sedating Therapy for Tourette Syndrome

RAP is indicated for patients who have failed to respond satisfactorily to standard treatment.
ase see following page for a brief summary of prescribing information.

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# ORAP™ The Less Sedating Therapy for Tourette Syndrome

## (pimozide) Tablets

### INDICATIONS AND USAGE

ORAP (pimozide) is indicated for the suppression of motor and phonic tics in patients with Tourette's Disorder who have failed to respond satisfactorily to standard treatment. ORAP is not intended as a treatment of first choice nor is it intended for the treatment for tics that are merely annoying or cosmetically troublesome. ORAP should be reserved for use in Tourette's Disorder patients whose development and/or daily life function is severely compromised by the presence of motor and phonic tics.

Evidence supporting approval of pimozide for use in Tourette's Disorder was obtained in two controlled clinical investigations which enrolled patients between the ages of 8 and 53 years. Most subjects in the two trials were 12 or older.

### CONTRAINDICATIONS

1. ORAP (pimozide) is contraindicated in the treatment of simple tics or tics other than associated with Tourette's Disorder.
2. ORAP should not be used in patients taking drugs that may, themselves, cause motor and phonic tics (e.g., pemoline, methylphenidate and amphetamines) until such patients have been withdrawn from these drugs to determine whether or not the drugs, rather than Tourette's Disorder, are responsible for the tics.
3. Because ORAP prolongs the QT interval of the electrocardiogram it is contraindicated in patients with congenital long QT syndrome, patients with a history of cardiac arrhythmias, or patients taking other drugs which prolong the QT interval of the electrocardiogram (see DRUG INTERACTIONS).
4. ORAP is contraindicated in patients with severe toxic central nervous system depression or comatose states from any cause.
5. ORAP is contraindicated in patients with hypersensitivity to it. As it is not known whether cross-sensitivity exists among the antipsychotics, pimozide should be used with appropriate caution in patients who have demonstrated hypersensitivity to other antipsychotic drugs.

### WARNINGS

The use of ORAP (pimozide) in the treatment of Tourette's Disorder involves different risk/benefit considerations than when antipsychotic drugs are used to treat other conditions. Consequently, a decision to use ORAP should take into consideration the following: (see also PRECAUTIONS–Information for Patients).

*Tardive Dyskinesia* A syndrome consisting of potentially irreversible, involuntary, dyskinetic movements may develop in patients treated with antipsychotic drugs. Although the prevalence of the syndrome appears to be highest among the elderly, especially elderly women, it is impossible to rely upon prevalence estimates to predict, at the inception of antipsychotic treatment, which patients are likely to develop the syndrome. Whether antipsychotic drug products differ in their potential to cause tardive dyskinesia is unknown.

Both the risk of developing tardive dyskinesia and the likelihood that it will become irreversible are believed to increase as the duration of treatment is withdrawn. Antipsychotic treatment, itself, however, may suppress (or partially suppress) the signs and symptoms of the syndrome and thereby may possibly mask the underlying process. The effect that symptomatic suppression has upon the long-term course of the syndrome is unknown.

Given these considerations, antipsychotic drugs should be prescribed in a manner that is most likely to minimize the occurrence of tardive dyskinesia. Chronic antipsychotic treatment should generally be reserved for patients who suffer from a chronic illness that, 1) is known to respond to antipsychotic drugs, and, 2) for whom alternative, equally effective, but potentially less harmful treatments are not available or appropriate. In patients who do require chronic treatment, the smallest dose and the shortest duration of treatment producing a satisfactory clinical response should be sought. The need for continued treatment should be reassessed periodically.

If signs and symptoms of tardive dyskinesia appear in a patient on antipsychotics, drug discontinuation should be considered. However, some patients may require treatment despite the presence of the syndrome.

(For further information about the description of tardive dyskinesia and its clinical detection, please refer to ADVERSE REACTIONS and PRECAUTIONS–Information for Patients.)

*Neuroleptic Malignant Syndrome (NMS)* A potentially fatal symptom complex sometimes referred to as Neuroleptic Malignant Syndrome (NMS) has been reported in association with antipsychotic drugs. Clinical manifestations of NMS are hyperpyrexia, muscle rigidity, altered mental status (including catatonic signs) and evidence of autonomic instability (irregular pulse or blood pressure, tachycardia, diaphoresis, and cardiac dysrhythmias). Additional signs may include elevated creatine phosphokinase, myoglobinuria (rhabdomyolysis) and acute renal failure.

The diagnostic evaluation of patients with this syndrome is complicated. In arriving at a diagnosis, it is important to identify cases where the clinical presentation includes both serious medical illness (e.g., pneumonia, systemic infection, etc.) and untreated or inadequately treated extrapyramidal signs and symptoms (EPS). Other important considerations in the differential diagnosis include central anticholinergic toxicity, heat stroke, drug fever and primary central nervous system (CNS) pathology.

The management of NMS should include 1) immediate discontinuation of antipsychotic drugs and other drugs not essential to concurrent therapy, 2) intensive symptomatic treatment and medical monitoring, and 3) treatment of any concomitant serious medical problems for which specific treatments are available. There is no general agreement about specific pharmacological treatment regimens for uncomplicated NMS.

If a patient requires antipsychotic drug treatment after recovery from NMS, the potential reintroduction of drug therapy should be carefully considered. The patient should be carefully monitored, since recurrences of NMS have been reported.

Hyperpyrexia, not associated with the above symptom complex, has been reported with other antipsychotic drugs.

*Other* Sudden, unexpected deaths have occurred in experimental studies of conditions other than Tourette's Disorder. These deaths occurred while patients were receiving dosages in the range of 1 mg per kg. One possible mechanism for such deaths is prolongation of the QT interval predisposing patients to ventricular arrhythmia. An electrocardiogram should be performed before ORAP treatment is initiated and periodically thereafter, especially during the period of dose adjustment.

ORAP may have a tumorigenic potential. Based on studies conducted in mice, it is known that pimozide can produce a dose related increase in pituitary tumors. The full significance of this finding is not known, but should be taken into consideration in the physician's and patient's decisions to use this drug product. This finding should be given special consideration when the patient is young and chronic use of pimozide is anticipated. (see PRECAUTIONS–Carcinogenesis, Mutagenesis, Impairment of Fertility).

### PRECAUTIONS

*General* ORAP (pimozide) may impair the mental and/or physical abilities required for the performance of potentially hazardous tasks, such as driving a car or operating machinery, especially during the first few days of therapy.

ORAP produces anticholinergic side effects and should be used with caution in individuals whose conditions may be aggravated by anticholinergic activity.

ORAP should be administered cautiously to patients with impairment of liver or kidney function, because it is metabolized by the liver and excreted by the kidneys.

Antipsychotics should be administered with caution to patients receiving anticonvulsant medication, with a history of seizures, or with EEG abnormalities, because they may lower the convulsive threshold. If indicated, adequate anticonvulsant therapy should be maintained concomitantly.

*Laboratory Tests* An ECG should be done at baseline and periodically thereafter throughout the period of dose adjustment. Any indication of prolongation of $QT_C$ interval beyond an absolute limit of 0.47 seconds (children) or 0.52 seconds (adults), or more than 25% above the patient's original baseline should be considered a basis for stopping further dose increase (see CONTRAINDICATIONS) and considering a lower dose.

Since hypokalemia has been associated with ventricular arrhythmias, potassium insufficiency, secondary to diuretics, diarrhea, or other cause, should be corrected before ORAP therapy is initiated and normal potassium maintained during therapy.

*Drug Interactions* Because ORAP prolongs the QT interval of the electrocardiogram, an additive effect on QT interval would be anticipated if administered with other drugs, such as phenothiazines, tricyclic antidepressants or antiarrhythmic agents, which prolong the QT interval. Such concomitant administration should not be undertaken (see CONTRAINDICATIONS).

ORAP may be capable of potentiating CNS depressants, including analgesics, sedatives, anxiolytics, and alcohol.

*Carcinogenesis, Mutagenesis, Impairment of Fertility* Carcinogenicity studies were conducted in mice and rats. In mice, pimozide causes a dose-related increase in pituitary and mammary tumors.

When mice were treated for up to 18 months with pimozide, pituitary gland changes developed in females only. These changes were characterized as hyperplasia at doses approximating the human dose and adenoma at doses about fifteen times the maximum recommended human dose on a mg per kg basis. The mechanism for the induction of pituitary tumors in mice is not known.

Mammary gland tumors in female mice were also increased, but these tumors are expected in rodents treated with antipsychotic drugs which elevate prolactin levels. Chronic administration of an antipsychotic also causes elevated prolactin levels in humans. Tissue culture experiments indicate that approximately one-third of human breast cancers are prolactin-dependent in vitro, a factor of potential importance if the prescription of these drugs is contemplated in a patient with a previously detected breast cancer. Although disturbances such as galactorrhea, amenorrhea, gynecomastia, and impotence have been reported with antipsychotic drugs, the clinical significance of elevated serum prolactin levels is unknown for most patients. Neither clinical studies nor epidemiologic studies conducted to date have shown an association between chronic administration of these drugs and mammary tumorigenesis. The available evidence, however, is considered too limited to be conclusive at this time.

In a 24 month carcinogenicity study in rats, animals received up to 50 times the maximum recommended human dose. No increased incidence of overall tumors or tumors at any site was observed in either sex. Because of the limited number of animals surviving this study, the meaning of these results is unclear.

Pimozide did not have mutagenic activity in the Ames test with four bacterial test strains, in the mouse dominant lethal test or in the micronucleus test in rats.

Reproduction studies in animals were not adequate to assess all aspects of fertility. Nevertheless, female rats administered pimozide had prolonged estrus cycles, an effect also produced by other antipsychotic drugs.

*Pregnancy Category C.* Reproduction studies performed in rats and rabbits at oral doses up to 8 times the maximum human dose did not reveal evidence of teratogenicity. In the rat, however, this multiple of the human dose resulted in decreased pregnancies and in the retarded development of fetuses. These effects are thought to be due to an inhibition or delay in implantation which is also observed in rodents administered other antipsychotic drugs. In the rabbit, maternal toxicity, mortality, decreased weight gain, and embryotoxicity including increased resorptions were dose related. Because animal reproduction studies are not always predictive of human response, pimozide should be given to a pregnant woman only if the potential benefits of treatment clearly outweigh the potential risks.

*Labor and Delivery* This drug has no recognized use in labor or delivery.

*Nursing Mothers* It is not known whether pimozide is excreted in human milk. Because many drugs are excreted in human milk and because of the potential for tumorigenicity and unknown cardiovascular effects in the infant, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

*Pediatric Use* Although Tourette's Disorder most often has its onset between the ages of 2 and 15 years, information on the use and efficacy of ORAP in patients less than 12 years of age is limited.

Because its use and safety have not been evaluated in other childhood disorders, ORAP is not recommended for use in any condition other than Tourette's Disorder.

### ADVERSE REACTIONS

*General: Extrapyramidal Reactions:* Neuromuscular (extrapyramidal) reactions during the administration of ORAP (pimozide) have been reported frequently, often during the first few days of treatment. In most patients, these reactions involved Parkinson-like symptoms which, when first observed, were usually mild to moderately severe and usually reversible.

Other types of neuromuscular reactions (motor restlessness, dystonia, akathisia, hyperreflexia, opisthotonos, oculogyric crises) have been reported far less frequently. Severe extrapyramidal reactions have been reported to occur at relatively low doses. Generally the occurrence and severity of most extrapyramidal symptoms are dose related since they occur at relatively high doses and have been shown to disappear or become less severe when the dose is reduced. Administration of antiparkinson drugs such as benztropine mesylate or trihexyphenidyl hydrochloride may be required for control of such reactions. It should be noted that persistent extrapyramidal reactions have been reported and that the drug may have to be discontinued in such cases.

*Withdrawal Emergent Neurological Signs:* Generally, patients receiving short term therapy experience no problems with abrupt discontinuation of antipsychotic drugs. However, some patients on maintenance treatment experience transient dyskinetic signs after abrupt withdrawal. In certain of these cases the dyskinetic movements are indistinguishable from the syndrome described below under 'Tardive Dyskinesia' except for duration. It is not known whether gradual withdrawal of antipsychotic drugs will reduce the rate of occurrence of withdrawal emergent neurological signs but until further evidence becomes available, it seems reasonable to gradually withdraw use of ORAP.

*Tardive Dyskinesia:* ORAP may be associated with persistent dyskinesias. Tardive dyskinesia, a syndrome consisting of potentially irreversible, involuntary, dyskinetic movements, may appear in some patients on long-term therapy or may occur after drug therapy has been discontinued. The risk appears to be greater in elderly patients on high-dose therapy, especially females. The symptoms are persistent and in some patients appear irreversible. The syndrome is characterized by rhythmical involuntary movements of tongue, face, mouth or jaw (e.g., protrusion of tongue, puffing of cheeks, puckering of mouth, chewing movements). Sometimes these may be accompanied by involuntary movements of extremities and the trunk.

There is no known effective treatment for tardive dyskinesia; antiparkinson agents usually do not alleviate the symptoms of this syndrome. It is suggested that all antipsychotic agents be discontinued if these symptoms appear. Should it be necessary to reinstitute treatment, or increase the dosage of the agent, or switch to a different antipsychotic agent, this syndrome may be masked.

It has been reported that fine vermicular movement of the tongue may be an early sign of tardive dyskinesia and if the medication is stopped at that time the syndrome may not develop.

*Electrocardiographic Changes:* Electrocardiographic changes have been observed in clinical trials of ORAP in Tourette's Disorder and schizophrenia. These have included prolongation of the QT interval, flattening, notching and inversion of the T wave and the appearance of U waves. Sudden, unexpected deaths and grand mal seizure have occurred at doses above 20 mg/day

*Neuroleptic Malignant Syndrome:* Neuroleptic malignant syndrome (NMS) has been reported with ORAP. (See WARNINGS for further information concerning NMS.)

*Hyperpyrexia:* Hyperpyrexia has been reported with other antipsychotic drugs.

*Clinical Trials* The following adverse reaction tabulation was derived from 20 patients in a 6 week long placebo controlled clinical trial of ORAP in Tourette's Disorder.

| Body System/ Adverse Reaction | Pimozide (N = 20) | Placebo (N = 20) |
|---|---|---|
| Body as a Whole | | |
| Headache | 1 | 2 |
| Gastrointestinal | | |
| Dry mouth | 5 | 1 |
| Diarrhea | 1 | 0 |
| Nausea | 0 | 2 |
| Vomiting | 0 | 1 |
| Constipation | 4 | 2 |
| Eructations | 0 | 1 |
| Thirsty | 1 | 0 |
| Appetite increase | 1 | 0 |
| Endocrine | | |
| Menstrual disorder | 0 | 1 |
| Breast secretions | 0 | 1 |
| Musculoskeletal | | |
| Muscle cramps | 0 | 1 |
| Muscle tightness | 3 | 0 |
| Stooped posture | 2 | 0 |
| CNS | | |
| Drowsiness | 7 | 3 |
| Sedation | 14 | 5 |
| Insomnia | 2 | 2 |
| Dizziness | 0 | 1 |
| Akathisia | 8 | 0 |
| Rigidity | 2 | 0 |
| Speech disorder | 2 | 0 |
| Handwriting change | 1 | 0 |
| Akinesia | 8 | 0 |
| Psychiatric | | |
| Depression | 2 | 3 |
| Excitement | 0 | 1 |
| Nervous | 1 | 0 |
| Adverse behavior effect | 5 | 0 |
| Special Sense | | |
| Visual disturbance | 4 | 0 |
| Taste change | 1 | 0 |
| Sensitivity of eyes to light | 1 | 0 |
| Decreased accommodation | 4 | 1 |
| Spots before eyes | 0 | 1 |
| Urogenital | | |
| Impotence | 3 | 0 |

Because clinical investigational experience with ORAP in Tourette's Disorder is limited, uncommon adverse reactions may not have been detected. The physician should consider that other adverse reactions associated with antipsychotics may occur.

*Other Adverse Reactions* In addition to the adverse reactions listed above, those listed below have been reported in U.S. clinical trials of ORAP in conditions other than Tourette's Disorder.

*Body as a Whole:* Asthenia, chest pain, periorbital edema

*Cardiovascular/Respiratory:* Postural hypotension, hypotension, hypertension, tachycardia, palpitations

*Gastrointestinal:* Increased salivation, nausea, vomiting, anorexia, GI distress

*Endocrine:* Loss of libido

*Metabolic/Nutritional:* Weight gain, weight loss

*Central Nervous System:* Dizziness, tremor, parkinsonism, fainting, dyskinesia

*Psychiatric:* Excitement

*Skin:* Rash, sweating, skin irritation

*Special Senses:* Blurred vision, cataracts

*Urogenital:* Nocturia, urinary frequency

*Postmarketing Reports* The following experiences were described in spontaneous postmarketing reports. These reports do not provide sufficient information to establish a clear causal relationship with the use of ORAP.

*Hematologic:* Hemolytic anemia

### OVERDOSAGE

In general, the signs and symptoms of overdosage with ORAP (pimozide) would be an exaggeration of known pharmacologic effects and adverse reactions, the most prominent of which would be: 1) electrocardiographic abnormalities, 2) severe extrapyramidal reactions, 3) hypotension, 4) a comatose state with respiratory depression.

In the event of overdosage, gastric lavage, establishment of a patent airway and, if necessary mechanically-assisted respiration are advised. Electrocardiographic monitoring should commence immediately and continue until the ECG parameters are within the normal range. Hypotension and circulatory collapse may be counteracted by use of intravenous fluids, plasma, or concentrated albumin, and vasopressor agents such as metaraminol, phenylephrine and norepinephrine. Epinephrine should not be used. In case of severe extrapyramidal reactions, antiparkinson medication should be administered. Because of the long half-life of pimozide, patients who take an overdose should be observed for at least 4 days. As with all drugs, the physician should consider contacting a poison control center for additional information on the treatment of overdose.

### DOSAGE AND ADMINISTRATION

Reliable dose response data for the effects of ORAP (pimozide) on tic manifestations in Tourette's Disorder patients below the age of twelve are not available. Consequently, the suppression of tics by ORAP requires a slow and gradual introduction of the drug. The patient's dose should be carefully adjusted to a point where the suppression of tics and the relief afforded is balanced against the untoward side effects of the drug.

An ECG should be done at baseline and periodically thereafter, especially during the period of dose adjustment (see WARNINGS and PRECAUTIONS–Laboratory Tests).

In general, treatment with ORAP should be initiated with a dose of 1 to 2 mg a day in divided doses. The dose may be increased thereafter every other day. Most patients are maintained at less than 0.2 mg/kg per day, or 10 mg/day, whichever is less. Doses greater than 0.2 mg/kg/day or 10 mg/day are not recommended.

Periodic attempts should be made to reduce the dosage of ORAP to see whether or not tics persist at the level and extent first identified. In attempts to reduce the dosage of ORAP, consideration should be given to the possibility that increases of tic intensity and frequency may represent a transient, withdrawal related phenomenon rather than a return of disease symptoms. Specifically, one to two weeks should be allowed to elapse before one concludes that an increase in tic manifestations is a function of the underlying disease syndrome rather than a response to drug withdrawal. A gradual withdrawal is recommended in any case.

### HOW SUPPLIED

ORAP (pimozide) 2 mg tablets, white, scored, imprint 'LEMMON' and 'ORAP 2'–NDC 0093-0187-01, bottles of 100.

Dispense in tight, light-resistant containers as defined in the official compendium.

Made in Canada

Manufactured by:
McNeil Pharmaceutical, (Canada) Ltd.
Stouffville, Ontario L4A 7x7

Printed in USA
Rev. A 6/88

Manufactured for:
LEMMON COMPANY
Sellersville, PA 18960

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1. Shapiro AK et al: *Pediatrics* 79:1032-1038, 1987.
2. Ross MS et al: *Am J Psychiatry* 135:585-587, 1978.

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# Information for Contributors

## GENERAL POLICIES

The requirements stated below are in accordance with "Uniform Requirements for Manuscripts Submitted to Biomedical Journals."

### Prior Publication

Manuscripts are accepted for consideration by the *American Journal of Psychiatry* with the understanding that they represent original material, have not been published previously, are not being considered for publication elsewhere, and have been approved by each author. Any form of publication other than an abstract of no more than 400 words constitutes prior publication. This includes components of symposia, proceedings, transactions, books (or chapters), articles published by invitation, or reports of any kind, regardless of differences in readership, as well as electronic data bases of public nature. Authors submitting manuscripts containing data or clinical observations already used in published papers or used in papers that are in press, submitted for publication, or to be submitted shortly should provide this information and copies of those papers to the Editor. An explanation of the differences between the papers should be included.

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In addition, authors must obtain letters of permission from publishers for use of extensive quotations (more than 500 words). The *Journal* does not publish tables or figures that have been previously published or submitted elsewhere.

### Disclosure of Commercial Interests

All forms of support, including drug company support, must be acknowledged in the author's footnote (see "Acknowledgments" under the Title Page section). Also, authors must disclose in their cover letter any commercial or financial involvements that might present an appearance of a conflict of interest in connection with the submitted article, including but not limited to institutional or corporate affiliations not already specified in the author's footnote, paid consultancies, stock ownership or other equity interests, and patent ownership. At the Editor's discretion, this information may be shared with reviewers. Such involvements will not be grounds for automatic rejection of the manuscript. Should the article be accepted for publication, the Editor and the authors will consult on whether, and to what extent, this information should be included in the published article.

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Ethical as well as legal considerations require careful attention to the protection of a patient's anonymity in case reports and elsewhere. Identifying information such as names, initials, hospital numbers, and dates must be avoided. In addition, authors should disguise identifying information when discussing the characteristics and personal history of patients.

### Informed Consent

Manuscripts that report the results of experimental investigation with human subjects must include a statement that informed consent was obtained after the procedure(s) had been fully explained. In the case of children, authors are asked to include information about whether the child's assent was obtained.

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All papers are reviewed to determine the originality, validity, and importance of content and conclusions. In addition to the regular review process, peer review for statistical content may be required for some manuscripts. This will be determined by the *Journal*'s Statistical Editors. Authors will be sent reviewer comments that are judged to be useful to them. All reviewers remain anonymous. Once the Editor has made a final decision on a paper, the authors of that paper will be informed.

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The original manuscript and four copies should be submitted to John C. Nemiah, M.D., Editor, *American Journal of Psychiatry*, 1400 K St., N.W., Washington, DC 20005. All correspondence will be sent to the first-named author unless otherwise specified. Papers should be accompanied by a cover letter indicating that the paper is intended for publication and specifying for which section of the *Journal* it is being submitted (i.e., Special Article, Regular Article, or Clinical and Research Report); papers will only be reviewed after such a statement has been received from the author.

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Single case reports except for detailed longitudinal studies should be submitted as Letters to the Editor. All single case reports will be peer reviewed. Reports of successfully treated patients must include data on the number of patients treated unsuccessfully by the same method, with an indication of the temporal order of the successes and failures.

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Authors may submit their papers before the annual meeting, but such papers cannot be published until after the meeting. All papers must be accompanied by a statement that they are in final form. These papers are subject to the same peer review as other papers and must conform to the requirements for one of the types of articles specified in the next section.

## TYPES OF ARTICLES

### Special Articles

These are usually overview articles that bring together important information on a topic of general interest to psychiatry. Authors who have ideas for such articles are advised to check with the Editorial Office to ensure that a similar work has not already been submitted. Special Articles may not exceed 7,500 words (no more than 25 double-spaced pages—including an abstract of no more than 100 words, tables, and figures) and may not include more than 100 references.

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Regular Articles are original communications of scientific excellence in psychiatric medicine and advances in clinical research. Regular Articles contain no more than 3,800 words, including an abstract of no more than 100 words, references, tables, and figures. A table or figure that fills one-half of a vertical manuscript page equals 100 words of text; one that fills one-half of a horizontal page equals 150 words. Articles that exceed 3,800 words will be returned unreviewed to the authors.

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Clinical and Research Reports may contain no more than one table and a maximum of 10 references; figures may not be used. Papers may contain a **maximum** of 1,300 words, including an abstract of no more than 40 words, references, and an optional table (estimate 15 words per reference, 100 words for a double-spaced table that fills one-half of a vertical page, and 150 words for a double-spaced table that fills one-half of a horizontal page). These articles present 1) new research findings, 2) data from pilot studies, 3) worthwhile replication studies, and 4) clinical studies involving a number of patients. Essays, program descriptions, literature reviews, and single case reports do not meet the criteria for this section. Submissions that exceed 1,300 words or contain figures will be returned to the author.

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**Book Forum.** Books for review may be sent to the Book Forum Editor, Nancy C. Andreasen, M.D., Ph.D., University of Iowa College of Medicine, 500 Newton Rd., Iowa City, IA 52242. Book reviews are usually solicited by the Book Forum Editor. Authors interested in reviewing a particular book should communicate directly with Dr. Andreasen. Reprints of reviews are not available.

## TYPING AND ARRANGING THE PAPER

All parts of the manuscript, including case reports, quotations, references, and tables, must be **double-spaced** throughout. Manuscripts must be typed in upper- and lowercase on one side only of 8½×11 inch **nonerasable** bond paper. All four margins must be 1½ inches. The manuscript should be arranged in the following order, with each item beginning a new page: 1) title page, 2) abstract, 3) text, 4) references, and 5) tables and/or figures. All pages must be numbered.

## STYLE SPECIFICATIONS

### Title Page

**Title.** The title should be informative and as brief as possible. Two-part titles should be avoided.

**By-line.** Authors listed in the by-line should be limited to principal researchers and/or writers; collaborators may be acknowledged in a footnote. Authors' first names are preferred to initials. Degrees should be included after each author's name.

**Previous presentation.** If the paper has been presented at a meeting, please give the name of the meeting, the place, and the date.

**Location of work and address for reprints.** Provide the department, institution, city, and state **where the work was done.** Include a full address for the author who is to receive reprint requests.

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### Abstract

The abstract is a single paragraph no longer than 100 words for Special Articles and Regular Articles and no longer than 40 words for Clinical and Research Reports.

### Text

Authors should use the active voice and first person; headings and subheadings should be inserted at reasonable intervals. Footnotes to text may not be used, and summaries are usually unnecessary.

**Research design and statistics.** The following information regarding research design should be included: 1) a clearly stated hypothesis, 2) the names of the statistical tests used, 3) whether tests were one- or two-tailed, and 4) what test was used for each set of data. Reporting of standard deviations, rather than standard errors of the mean, is required. Statistical tests that are not well known should be referenced. **All** significant and important nonsignificant results must include the test value, degree(s) of freedom, and probability. For example, "The analysis of variance indicated that those who abstained from coffee had significantly higher course grades than those who did not abstain ($F=4.32$, $df=3, 17$, $p< 0.05$)." Reviewers will evaluate the appropriateness of the analyses.

**Abbreviations.** Spell out all abbreviations (other than those for units of measure) the first time they are used. Idiosyncratic abbreviations should not be used.

**Drugs.** Generic rather than trade names of drugs should be used. Trade or manufacturers' names are used only if the drug or equipment is experimental or unavailable in this country or if such information is crucial to the evaluation of the results or replication of the study.

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References are numbered and listed by their order of appearance in text; the text citation is followed by the appropriate reference number in parentheses. Do **not** arrange the list alphabetically. References in tables and figures are numbered as though the tables and figures were part of the text.

References should be restricted to closely pertinent material. **Accuracy of citation is the author's responsibility.** References should conform exactly to the original spelling, accents, punctuation, etc. Authors should be sure that all references listed have been cited in text.

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2. Kaplan HI, Sadock BJ (eds): Comprehensive Textbook of Psychiatry, 4th ed, vol 2. Baltimore, Williams & Wilkins, 1985
3. Fyer AJ, Manuzza S, Endicott J: Differential diagnosis and assessments of anxiety: recent developments, in Psychopharmacology: The Third Generation of Progress. Edited by Meltzer HY. New York, Raven Press, 1987

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### Tables

**Tables should be double-spaced, no wider than 120 typewriter characters, including spaces, and no longer than 70 lines.** Values expressed in the same unit of measurement should read down, not across; when percentages are given, the appropriate numbers must also be given.

### Figures

Figures are considered as text and are subject to revision by the authors upon recommendation of the Editors. Figures should, however, be professionally prepared. Glossy or other camera-ready prints should accompany the submitted manuscript. Computer-generated figures that do not meet quality printing standards will be returned for revision. The first author's name, the title of the paper, the figure number, and the top of the figure should be noted on a label affixed to the back of each figure. All figure titles and footnotes should be typed and sent together on a separate page.

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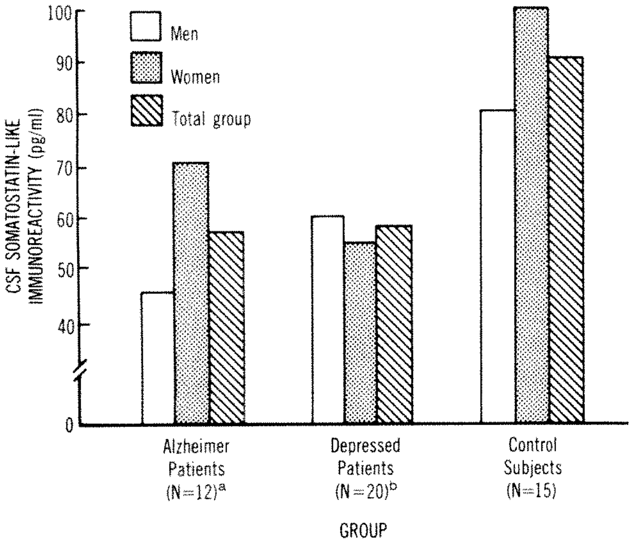
**Format.** Figures are visual expressions of data trends or relationships. Figures that represent numerical data which could be expressed more succinctly or clearly in tabular form should be converted to tables. Line graphs should show change in continuous variables; comparisons of like values in different groups should be presented as bar graphs. Graphs containing stacked bars are unacceptable; the different segments of each bar should be presented side by side.

**Lettering.** Figure type should be sans serif and should be 7 points or larger after the figure is reduced; most figures taking up the width of a vertical manuscript page are reduced to a width of 19.5 picas (3¼ inches), and those requiring a horizontal manuscript page are usually reduced to 40.5 picas (6¾ inches). When space on the horizontal axis is insuffi-

**FIGURE 1. Mean CSF Somatostatin Levels of Patients With Alzheimer's Disease, Older Depressed Patients, and Age-Matched Control Subjects**



[a] Significant difference between men and women ($t=1.81$, $df=10$, $p<0.05$) and between the total Alzheimer's disease group and the total control group ($t=2.49$, $df=25$, $p<0.01$).

[b] Significant difference between the total depressed group and the total control group ($t=2.75$, $df=33$, $p<0.005$).

cient, headings may be placed diagonally on the axis. Main headings should consist of upper-case letters only, subheadings of upper- and lower-case, and other type (e.g., keys, flow chart segments) of lower-case with only an initial upper-case letter. All parenthetical material should be lower-case. Do not use idiosyncratic abbreviations.

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5. The vertical axis should generally begin at zero; to save space, a double slash may take the place of an unused portion of the vertical axis.
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7. To save space, related figures that have the same vertical or horizontal axis should be combined. Headings identifying the segments of the combined figure should appear in the upper lefthand corners of the individual segments (in lower-case type with an initial upper-case letter).
8. The key should appear within or above the figure but should not be wider than the figure itself. Avoid placing other type (e.g., number of subjects, statistical values) within the axes of a graph.
9. Footnotes (including p values) should be cited with superscript letters in the title or body of the figure and should be listed in the order in which they are cited in the figure.

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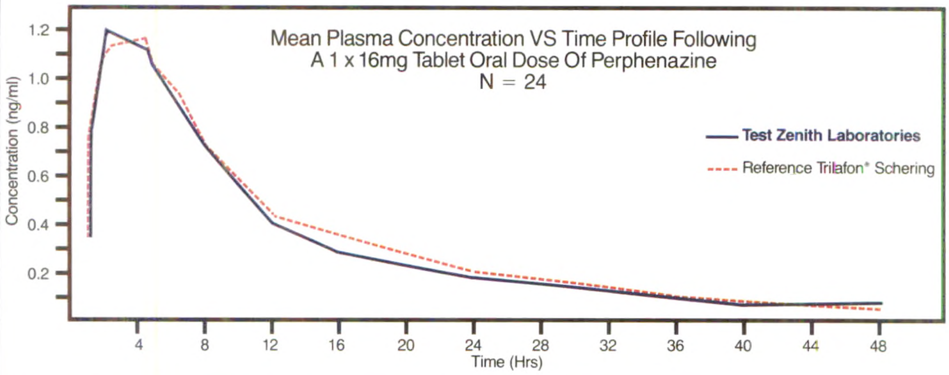

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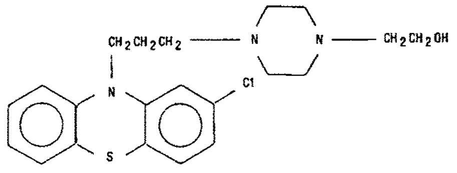
# PERPHENAZINE TABLETS, USP

## DESCRIPTION

Perphenazine (4-[3-(2-chlorophenothiazin-10-yl)propyl]-1-piperazineethanol), is a piperazinyl phenothiazine having the chemical formula, $C_{21}H_{26}ClN_3OS$ It is available as oral tablets, containing 2 mg, 4 mg, 8 mg, and 16 mg of perphenazine.

Inactive ingredients: acacia, carnauba wax, corn starch, FD&C Blue No 2, FD&C Yellow No 6, gelatin, lactose magnesium stearate, microcrystalline cellulose, povidone, precipitated calcium carbonate, pregelatinized starch, sodium benzoate, sodium starch glycolate, stearic acid, sucrose, talc, titanium dioxide, and white wax Its structural formula is:



## CLINICAL PHARMACOLOGY

Perphenazine has actions at all levels of the central nervous system, particularly the hypothalamus. However, the site and mechanism of action of therapeutic effect are not known.

## INDICATIONS

Perphenazine is indicated for use in the management of the manifestations of psychotic disorders; and for the control of severe nausea and vomiting in adults Perphenazine had not been shown effective in the management of behavioral complications in patients with mental retardation

## CONTRAINDICATIONS

Perphenazine products are contraindicated in comatose or greatly obtunded patients and in patients receiving large doses of central nervous system depressants (barbituates, alcohol, narcotics, analgesics, or antihistamines); in the presence of existing blood dyscrasias, bone marrow depression, or liver damage; and in patients who have shown hypersensitivity to perphenazine products, their components, or related compounds.

Perphenazine products are also contraindicated in patients with suspected or established subcortical brain damage, with or without hypothalamic damage, since a hyperthermic reaction with temperatures in excess of 104°F may occur in such patients, sometimes not until 14 to 16 hours after drug administration, since a hyperthermic reaction with temperatures in excess of 104°F may occur in such patients, sometimes not until 14 to 16 hours after drug administration. Total body ice-packing is recommended for such a reaction; antipyretics may also be used

## WARNINGS

Tardive dyskinesia, a syndrome consisting of potentially irreversible, involuntary, dyskinetic movements, may develop in patients treated with neuroleptic (antipsychotic) drugs. Although the prevalence of the syndrome appears to be highest among the elderly, especially elderly women, it is impossible to rely upon prevalence estimates to predict, at the inception of neuroleptic treatment, which patients are likely to develop the syndrome. Whether neuroleptic drug products differ in their potential to cause tardive dyskinesia is unknown

Both the risk of developing the syndrome and the likelihood that it will become irreversible are believed to increase as the duration of treatment and the total cumulative dose of neuroleptic drugs administered to the patient increase. However, the syndrome can develop, although much less commonly, after relatively brief treatment periods at low doses. There is no known treatment of established cases of tardive dyskinesia, although the syndrome may remit, partially or completely, if neuroleptic treatment is withdrawn. Neuroleptic treatment itself, however, may suppress (or partially suppress) the signs and symptoms of the syndrome, and thereby may possibly mask the underlying disease process. The effect that symptomatic suppression has upon the long-term course of the syndrome is unknown

Given these conditions, neuroleptics should be prescribed in a manner that is most likely to minimize the occurrence of tardive dyskinesia. Chronic neuroleptic treatment should generally be reserved for patients who suffer from a chronic illness that, 1) is known to respond to neuroleptic drugs, and 2) for whom alternative, equally effective, but potentially less harmful treatments are *not* available or appropriate. In patients who do require chronic treatment, the smallest dose and the shortest duration of treatment producing a satisfactory clinical response should be sought. The need for continued treatment should be reassessed periodically.

If signs and symptoms of tardive dyskinesia appear in a patient on neuroleptics, drug discontinuation should be considered. However, some patients may require treatment despite the presence of the syndrome

(For further information aobut the description of tardive dyskenesia and its clinical detection, please refer to **Information for Patients** and **ADVERSE REACTIONS.**)

**Neuroleptic Malignant Syndrome (NMS):** A potentially fatal symptom complex sometimes referred to as Neuroleptic Malignant Syndrome (NMS) has been reported in association with antipsychotic drugs. Clinical manifestations of NMS ar hyperpyrexia, muscle rigidity, altered mental status and evidence of autonomic instability (irregular pulse or blood pressure, tachycardia, diaphoresis, and cardiac dysrhythmias)

The diagnostic evaluation of patients with this syndrome is complicated. In arriving at a diagnosis, it is important to identify cases where the clinical presentation includes both serious medical illness (e.g., pneumonia, systemic infection, etc.) and untreated or inadequately treated extrapyramidal signs and symptoms (EPS). Other important considerations in the differential diagnosis include central anticholinergic toxicity, heat stroke, drug fever and primary central nervous system (CNS) pathology.

The management of NMS should include 1) immediate discontinuation of antipsychotic drugs and other drugs not essential to concurrent therapy, 2) intensive symptomatic treatment and medical monitoring, and 3) treatment of any concomitant serious medical problems for which specific treatments are available. There is no general agreement about specific pharmacological treatment regimens of uncomplicated NMS.

If a patient requires antipsychotic drug treatment after recovery from NMS, the potential reintroduction of drug therapy should be carefully considered The patient should be carefully monitored, since recurrences of NMS have been reported

If hypotension develops, epinephrine should not be administered since its action is blocked and partially reversed by perphenazine. If a vasopressor is needed, norepinephrine may be used. Severe, acute hypotension has occurred with the use of phenothiazines and is particularly likely to occur in patients with mitral insufficiency or pheochromocytoma. Rebound hypertension may occur in pheochromocytoma patients.

Perphenazine products can lower the convulsive threshold in susceptible individuals; they should be used with caution in alcohol withdrawal and in patients with convulsive disorders If the patient is being treated with an anticonvulsant agent, increased dosage of that agent may be required when perphenazine products are used concomitantly.

Perphenazine products should be used with caution in patients with psychic depression.

Perphenazine may impair the mental and/or physical abilities required for the performance of hazardous tasks such as driving a car or operating machinery; therefore, the patient should be warned accordingly.

Perphenazine products are not recommended for children under 12 years of age.

**Usage In Pregnancy:** Safe use of perphenazine during pregnancy and lactation has not been established, therefore, in administering the drug to pregnant patients, nursing mothers, or women who may become pregnant, the possible benefits must be weighed against the possible hazards to mother and child.

## PRECAUTIONS

The possibility of suicide in depressed patients remains during treatment and until significant remission occurs. This type of patient should not have access to large quantities of this drug.

As with all phenothiazine compounds, perphenazine should not be used indiscriminately. Caution should be observed in giving it to patients who have previously exhibited severe adverse reactions to other phenothiazines. Some of the untoward actions of perphenazine tend to appear more frequently when high doses are used. However, as with other phenothiazine compounds, patients receiving perhenazine products in any dosage should be kept under close supervision. Neuroleptic drugs elevate prolactin levels; the elevation persists during chronic administration. Tissue culture experiments indicate that approximately one-third of human breast cancers and prolactin dependent *in vitro*, a factor of potential importance if the prescription of these drugs is contemplated in a patient with a previously detected breast cancer. Although disturbances such as galactorrhea, amenorrhea, gynecomaslia, and impotence have been reported, the clinical significance of elevated serum prolactin levels is unknown for most patients. An increase in mammary neoplasms has been found in rodents after chronic administration of neuroleptic drugs. Neither clinical studies nor epidemiologic studies conducted to date, however, have shown an association between chronic administration of these drugs and mammary tumorigenesis; the available evidence is considered too limited to be conclusive at this time.

The antiemetic effect of perphenazine may obscure signs of toxicity due to overdosage of other drugs, or render more difficult the diagnosis of disorders such as brain tumors or intestinal obstruction.

A significant, not otherwise explained, rise in body temperature may suggest individual intolerance to perphenazine, in which case it should be discontinued. Patients on large doses of a phenothiazine drug who are undergoing surgery should be watched carefully for possible hypotensive phenomena. Moreover, reduced amounts of anesthetics or central nervous system depressants may be necessary.

Since phenothiazines and central nervous system depressants (opiates, analgesics, antihistamines, barbituates) can potentiate each other, less than the usual dosage of the added drug is recommended, and caution is advised, when they are administered concomitantly.

Use with caution in patients who are receiving atropine or related drugs because of additive anticholinergic effects and also in patients who will be exposed to extreme heat or phosphorus insecticides.

The use of alcohol should be avoided, since additive effects and hypotension may occur. Patients should be cautioned that their response to alcohol may be increased while they are being treated with perphenazine products. The risk of suicide and the danger of overdose may be increased in patients who use alcohol excessively due to its potentiation of the drug's effect.

Blood counts and hepatic and renal functions should be checked periodically The appearance of signs of blood dyscrasias requires the discontinuance of the drug and institution of appropriate therapy. If abnormalities in hepatic tests occur, phenothiazine treatment should be discontinued. Renal function in patients on long-term therapy should be monitored; if blood urea nitrogen (BUN) becomes abnormal, treatment with the drug whould be discontinued.

The use of phenothiazine derivatives in patients with diminished renal function should be undertaken with caution.

Use with caution in patients suffering from respiratory impairment due to acute pulmonary infections, or in chronic respiratory disorders such as severe asthma or emphysema.

In general, phenothiazines, including perphenazine, do not produce psychic dependence. Gastritis, nausea and vomiting, dizziness, and tremulousness have been reported following abrupt cessation of high-dose therapy Reports suggest that these symptoms can be reduced by continuing concomitant antiparkinson agents for several weeks after the phenothiazine is withdrawn

The possibility of liver damage, corneal and lenticular deposits, and irreversible dyskinesias should be kept in mind when patients are on long-term therapy. Because photosensitivity has been reported, undue exposure to the sun should be avoided during phenothiazine treatment.

**Information for Patients:** This information is intended to aid in the safe and effective use of this medication. It is not a disclosure of all possible adverse or intended effects.

Given the likelihood that a substantial proportion of patients exposed chronically to neuroleptics will develop tardive dyskinesia, it is advised that all patients in whom chronic use is contemplated be given, if possible, full information about this risk. The decision to inform patients and/or their guardians must obviously take into account the clinical circumstances and the competency of the patient to understand the information provided

## ADVERSE REACTIONS

Not all of the following adverse reactions have been reported with this specific drug; however, pharmacological similarities among various phenothiazine derivatives require that each be considered. In the case of the piperazine group (of which perphenazine is an example), the extrapyramidal symptoms are more common, and others (e.g., sedative effects, jaundice, and blood dyscrasias) are less frequently seen

**CNS Effects:** Extrapyramidal reactions: opisthotonus, trismus, torticollis, retrocollis, aching and numbness of the limbs, motor restlessness, oculogyric crisis, hyperreflexia, dystonia, including protrusion, discoloration, aching and rounding of the tongue, tonic spasm of the masticatory muscles, tight feeling in the throat, slurred speech, dysphagia, akathisia, dyskinesia, parkinsonism, and ataxia. Their incidence and severity usually increase with an increase in dosage, but there is considerable individual variation in the tendency to develop such symptoms. Extrapyramidal symptoms can usually be controlled by the concomitant use of effective antiparkinsonian drugs, such as benztropine mesylate, and/or by reduction in dosage. In some instances, however, these extrapyramidal reactions may persist after discontinuation of treatment with perphenazine.

**Persistent Tardive Dyskinesia:** As with all antipsychotic agents, tardive dyskinesia may appear in some patients on long-term therapy or may appear after drug therapy has been discontinued. Although the risk appears to be greater in elderly patients on high-dose therapy, especially females, it may occur in either sex and in children The symptoms are persistent and in some patients appear to be irreversible. The syndrome is characterized by rhythmical, involuntary movements of the tongue, face, mouth or jaw (e.g. protrusion of tongue, puffing of cheeks, puckering of mouth, chewing movements). Sometimes these may be accompanied by involuntary movements of the extremities. There is no known effective treatment for tardive dyskinesia, antiparkinsonism agents usually do not alleviate the symptoms of this syndrome. It is suggested that all antipsychotic agents be discontinued if these symptoms appear. Should it be necessary to reinstitute treatment, or increase the dosage of the agent, or switch to a different antipsychotic agent, the syndrome may be masked. It has been reported that fine, vermicular movements of the tongue may be an early sign of the syndrome, and if the medication is stopped at that time the syndrome may not develop. Other CNS effects include cerebral edema; abnormality of cerebrospinal fluid proteins; convulsive seizures, particularly in patients with EEG abnormalities or a history of such disorders; and headaches.

Neuroleptic malignant syndrome has been reported in patients treated with neuroleptic drugs. (see **WARNINGS**).

Drowsiness may occur, particularly during the first or second week, after which it generally disappears. If troublesome, lower the dosage. Hypnotic effects appear to be minimal, especially in patients who are permitted to remain active.

Adverse behavioral effects include paradoxical exacerbation of psychotic symptoms, catatonic-like states, paranoid reactions, lethargy, paradoxical excitment, restlessness, hyperactivity, nocturnal confusion, bizarre dreams, and insomnia.

Hyperreflexia has been reported in the newborn when a phenothiazine was used during pregnancy.

**Autonomic Effects:** dry mouth or salivation, nausea, vomiting, diarrhea, anorexia, constipation, obstipation, fecal impaction, urinary retention, frequency or incontinence, bladder paralysis, polyuria, nasal congestion, pallor, myosis, mydriasis, blurred vision, glaucoma, perspiration, hypertension, hypotension and change in pulse rate occasionally may occur. Significant autonomic effects have been infrequent in patients receiving less than 24 mg of perphenazine daily. Adynamic ileus occasionally occurs with phenothiazine therapy and if severe can result in complications and death. It is of particular concern in psychiatric patients, who may fail to seek treatment of the condition

**Allergic Effects.** urticaria, erythema, eczema, exfoliative dermatitis, pruritus, photosensitivity, asthma, fever, anaphylactoid reactions, laryngeal edema and angioneurotic edema, contact dermatitis in nursing personnel administering the drug, and in extremely rare instances, individual idiosyncrasy or hypersensitivity to phenothiazines has resulted in cerebral edema, circulatory collapse, and death.

**Endocrine Effects:** lactation, galatorrhea, moderate breast enlargement in females and gynecomastia in males on large doses, distrubances in the menstrual cycle, amenorrhea, changes in libido, inhibition of ejaculation, syndrome of inappropriate ADH (antidiuretic hormone) secretion, false positive pregnancy tests, hyperglycemia, hypoglycemia, glycosuria

**Cardiovascular Effects:** postural hypotension, tachycardia (especially with sudden marked increase in dosage), bradycardia, cardiac arrest, faintness, and dizziness. Occasionaly the hypotensive effect may produce a shock-like condition. ECG changes, nonspecific (quinidine-like effect) usually reversible, have been observed in some patients receiving phenothiazine tranquilizers.

Sudden death has occasionally been reported in patients who have received phenothiazines. In some cases the death was apparently due to cardiac arrest, in others, the cause appeared to be asphyxia due to failure of the cough reflex. In some patients, the cause could not be determined nor could it be established that the death was due to the phenothiazine.

**Hematological Effects:** agranulocytosis, eosinophilia, leukopenia, hemolytic anemia, thrombocytopenic purpura, and pancytopenia. Most cases of agranulcytosis have occurred between the fourth and tenth weeks of therapy. Patients should be watched closely especially during that period for the sudden appearance of sore throat or signs of infection. If white blood cells and differential cell counts show signficant cellular depression, discontinue the drug and start appropriate therapy. However, a slightly lowered white count is not in itself an indication to discontinue the drug.

**Other Effects:** Special considerations in long-term therapy include pigmentation of the skin, occurring chiefly in the exposed areas, ocular changes consisting of deposition of fine particulate matter in the cornea and lens, progressing in more severe cases to star-shaped lenticular opacities, epithelial keratopattues, and pigmentary retinopathy. Also noted: peripheral edema, reversed epinephrine effect, increase in PBI not attributable to an increase in thyroxine, parotid swelling (rare), hyperpyrexia, systemic lupus erythematosus-like syndrome, increases in appetite and weight, polyphagia, photophobia, and muscle weakness. Liver damage (biliary stasis) may occur. Jaundice may occur, usually between the second and fourth weeks of treatment and is regarded as a hypersensitivity reaction. Incidence is low. The clinical picture resembles infectious hepatitis but with laboratory features of obstructive jaundice. It is usually reversible, however, chronic jaundice has been reported.

## OVERDOSAGE

In the event of overdosage, emergency treatment should be started immediately. All patients suspected of having taken an overdose should be hospitalized as soon as possible.

**Manifestations:** Overdosage of perphenazine primarily involves the extrapyramidal mechanism and produces the same side effects described under **ADVERSE REACTIONS,** but to a more marked degree. It is usually evidenced by stupor or coma; children may have convulsive seizures.

**Treatment:** Treatment is symptomatic and supportive. There is no specific antidote. The patient should be induced to vomit even if emesis has occurred spontaneously. Pharmacologic vomiting by the administration of ipecac syrup is a preferred method. It should be noted that ipecac has a central mode of action in addition to its local gastric irritant properties, and the central mode of action may be blocked by the antiemetic effect of perphenazine products Vomiting should not be induced in patients with impaired consciousness. The action of ipecac is facilitated by physical activity and by the administration of 8 to 12 fluid ounces of water. If emesis does not occur within 15 minutes, the dose of ipecac should be repeated Precautions against aspiration must be taken, especially in infants and children. Following emesis any drug remaining in the stomach may be absorbed by activated charcoal administered as a slurry with water. If vomiting is unsuccessful or contraindicated, gastric lavage should be performed. Isotonic and one half isotonic saline are the lavage solutions of choice. Saline cathartics, such as milk of magnesia, draw water into the bowel by osmosis and therefore may be valuable for their action in rapid dilution of bowel content. Standard measures (oxygen, intravenous fluids, corticosteroids) should be used to manage circulatory shock or metabolic acidosis. An open airway and adequate fluid intake should be maintained. Body temperature should be regulated. Hypothermia is expected, but severe hyperthermia may occur and must be treated vigorously. (See **CONTRAINDICATIONS.**)

An electrocardiogram should be taken and close monitoring of cardiac function instituted if there is any sign of abnormality. Cardiac arrhythmias may be treated with neostigmine, pyridostigmine, or propranolol Digitalis should be considered for cardiac failure. Close monitoring of cardiac function is advisable for not less than five days. Vasopressors such as norepinephrine may be used to treat hypotension, but epinephrine should NOT be used.

Anticonvulsants (an inhalation anesthetic, diazepam, or paraldehyde) are recommended for control of convulsions, since perphenazine increases the central nervous system depressant action, but not the anticonvulsant action of barbiturates.

If acute parkinson-like symptoms result from perphenazine intoxication, benztropine mesylate or diphenhydramine may be administered.

Central nervous system depression may be treated with non-convulsant doses of CNS stimulants. Avoid stimulants that may cause convulsions (e.g. picrotoxin and pentylenetetrazol).

Signs of arousal may not occur for 48 hours.

Dialysis is of no value because of low plasma concentrations of the drug.

Since overdosage is often deliberate, patients may attempt suicide by other means during the recovery phase. Deaths by deliberate or accidental overdosage have occurred with this class of drug.

## DOSAGE AND ADMINISTRATION

Dosage must be individualized and adjusted according to the severity of the condition and the response obtained. As with all potent drugs, the best dose is the lowest dose that will produce the desired clinical effect. Since extrapyramidal symptoms increase in frequency and severity with increased dosage, it is important to employ the lowest effective dose. These symptoms have disappeared upon reduction of dosage, withdrawal of the drug or administration of an anti-parkinsonian agent.

Prolonged administration of doses exceeding 24 mg daily should be reserved for hospitalized patients or patients under continued observation for early detection and management of adverse reactions. An antiparkinsonian agent, such as trihexyphenidyl hydrochloride or benztropine mesylate, is valuable in controlling drug-induced extrapyramidal symptoms.

Suggested dosages for various conditions follow:

**Moderately disturbed non-hospitalized psychotic patients:** 4 to 8 mg t.i.d. initially, reduce as soon as possible to minimum effective dosage.

**Hospitalized psychotic patients:** 8 to 16 mg b.i.d. to q.i.d.; avoid dosages in excess of 64 mg daily.

**Severe nausea and vomiting in adults:** 8 to 16 mg daily in divided doses; 24 mg occasionally may be necessary; early dosage reduction is desirable.

## HOW SUPPLIED

Available as a round, gray tablet imprinted 3667/2 on one side and Zenith logo on opposite side containing 2 mg of perphenazine, USP, as a round gray tablet imprinted 3668/4 on one side and Zenith logo on opposite side containing 4 mg of perphenazine, USP, as a round, gray tablet imprinted 3669/8 on one side and Zenith logo on opposite side containing 8 mg of perphenazine, USP, as a round, gray tablet imprinted 3670/16 on one side and Zenith logo on opposite side containing 16 mg of perphenazine, USP. All strengths are packaged in bottles of 100 and 500 tablets.

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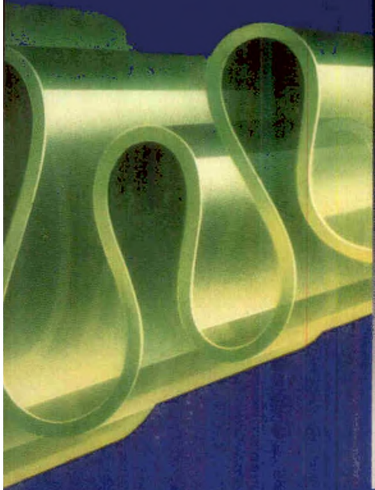

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**Warnings:** *Tardive Dyskinesia:* Tardive dyskinesia, a syndrome consisting of potentially irreversible, involuntary, dyskinetic movements may develop in patients treated with antipsychotic drugs. Although the prevalence of the syndrome appears to be highest among the elderly, especially elderly women, it is impossible to rely upon prevalence estimates to predict, at the inception of antipsychotic treatment, which patients are likely to develop the syndrome. Whether antipsychotic drug products differ in their potential to cause tardive dyskinesia is unknown. Both the risk of developing tardive dyskinesia and the likelihood that it will become irreversible are believed to increase as the duration of treatment and the total cumulative dose of antipsychotic drugs administered to the patient increase. However, the syndrome can develop, although much less commonly, after relatively brief treatment periods at low doses. There is no known treatment for established cases of tardive dyskinesia, although the syndrome may remit, partially or completely, if antipsychotic treatment is withdrawn. Antipsychotic treatment, itself, however, may suppress (or partially suppress) the signs and symptoms of the syndrome and thereby may possibly mask the underlying process. The effect that symptomatic suppression has upon the long-term course of the syndrome is unknown. Given these considerations, antipsychotic drugs should be prescribed in a manner that is most likely to minimize the occurrence of tardive dyskinesia. Chronic antipsychotic treatment should generally be reserved for patients who suffer from a chronic illness that 1) is known to respond to antipsychotic drugs, and 2) for whom alternative, equally effective, but potentially less harmful treatments are **not** available or appropriate. In patients who do require chronic treatment, the smallest dose and the shortest duration of treatment producing a satisfactory clinical response should be sought. The need for continued treatment should be reassessed periodically. If signs and symptoms of tardive dyskinesia appear in a patient on antipsychotics, drug discontinuation should be considered. However, some patients may require treatment despite the presence of the syndrome. (For further information about the description of tardive dyskinesia and its clinical detection, please refer to ADVERSE REACTIONS.)

*Neuroleptic Malignant Syndrome (NMS):* A potentially fatal symptom complex sometimes referred to as Neuroleptic Malignant Syndrome (NMS) has been reported in association with antipsychotic drugs. Clinical manifestations of NMS are hyperpyrexia, muscle rigidity, altered mental status (including catatonic signs) and evidence of autonomic instability (irregular pulse or blood pressure, tachycardia, diaphoresis, and cardiac dysrhythmias). Additional signs may include elevated creatine phosphokinase, myoglobinuria (rhabdomyolysis) and acute renal failure. The diagnostic evaluation of patients with this syndrome is complicated. In arriving at a diagnosis, it is important to identify cases where the clinical presentation includes both serious medical illness (e.g., pneumonia, systemic infection, etc.) and untreated or inadequately treated extrapyramidal signs and symptoms (EPS). Other important considerations in the differential diagnosis include central anticholinergic toxicity, heat stroke, drug fever and primary central nervous system (CNS) pathology. The management of NMS should include 1) immediate discontinuation of antipsychotic drugs and other drugs not essential to concurrent therapy, 2) intensive symptomatic treatment and medical monitoring, and 3) treatment of any concomitant serious medical problems for which specific treatments are available. There is no general agreement about specific pharmacological treatment regimens for uncomplicated NMS. If a patient requires antipsychotic drug treatment after recovery from NMS, the potential reintroduction of drug therapy should be carefully considered. The patient should be carefully monitored, since recurrences of NMS have been reported. Hyperpyrexia and heat stroke, not associated with the above symptom complex, have also been reported with HALDOL.

*Usage in Pregnancy:* (see PRECAUTIONS—Usage in Pregnancy) *Combined Use With Lithium:* (see PRECAUTIONS—Drug Interactions)

*General:* Bronchopneumonia sometimes fatal, has followed use of antipsychotic drugs, including haloperidol. Prompt remedial therapy should be instituted if dehydration, hemoconcentration or reduced pulmonary ventilation occur, especially in the elderly. Decreased serum cholesterol and/or cutaneous and ocular changes have been reported with chemically-related drugs, although not with haloperidol. See PRECAUTIONS—Information for Patients for information on mental and/or physical abilities and on concomitant use with other substances.

**Precautions:** Administer cautiously to patients: (1) with severe cardiovascular disorders, due to the possibility of transient hypotension and/or precipitation of anginal pain (if a vasopressor is required, epinephrine should not be used since HALDOL may block its vasopressor activity and paradoxical further lowering of blood pressure may occur; metaraminol, phenylephrine or norepinephrine should be used); (2) receiving anticonvulsant medications, with a history of seizures, or with EEG abnormalities, because HALDOL may lower the convulsive threshold. If indicated, adequate anticonvulsant therapy should be concomitantly maintained; (3) with known allergies or a history of allergic reactions to drugs; (4) receiving anticoagulants, since an isolated instance of interference occurred with the effects of one anticoagulant (phenindione). Concomitant antiparkinson medication, if required, may have to be continued after HALDOL is discontinued because of different excretion rates; if both are discontinued simultaneously, extrapyramidal symptoms may occur. Intraocular pressure may increase when anticholinergic drugs, including antiparkinson drugs, are administered concomitantly with HALDOL. When HALDOL is used for mania in bipolar disorders, there may be a rapid mood swing to depression. Severe neurotoxicity may occur in patients with thyrotoxicosis receiving antipsychotic medication, including HALDOL.

The 1, 5, 10 mg HALDOL tablets contain FD&C Yellow No. 5 (tartrazine) which may cause allergic-type reactions (including bronchial asthma) in certain susceptible individuals, especially in those who have aspirin hypersensitivity.

*Information for Patients:* Mental and/or physical abilities required for hazardous tasks or driving may be impaired. Alcohol should be avoided due to possible additive effects and hypotension.

*Drug Interactions:* Patients receiving lithium plus haloperidol should be monitored closely for early evidence of neurological toxicity and treatment discontinued promptly if such signs appear. As with other antipsychotic agents, it should be noted that HALDOL may be capable of potentiating CNS depressants such as anesthetics, opiates, and alcohol.

*Carcinogenesis, Mutagenesis and Impairment of Fertility:* No mutagenic potential of haloperidol decanoate was found in the Ames Salmonella microsomal activation assay.

Carcinogenicity studies using oral haloperidol were conducted in Wistar rats (dosed at up to 5 mg/kg daily for 24 months) and in Albino Swiss mice (dosed at up to 5 mg/kg daily for 18 months). In the rat study survival was less than optimal in all dose groups, reducing the number of rats at risk for developing tumors. However, although a relatively greater number of rats survived to the end of the study in high dose male and female groups, these animals did not have a greater incidence of tumors than control animals. Therefore, although not optimal, this study does suggest the absence of a haloperidol related increase in the incidence of neoplasia in rats at doses up to 20 times the usual daily human dose for chronic or resistant patients. In female mice at 5 and 20 times the highest initial daily dose for chronic or resistant patients, there was a statistically significant increase in mammary gland neoplasia and total tumor incidence; at 20 times the same daily dose there was a statistically significant increase in pituitary gland neoplasia. In male mice, no statistically significant differences in incidences of total tumors or specific tumor types were noted.

Antipsychotic drugs elevate prolactin levels; the elevation persists during chronic administration. Tissue culture experiments indicate that approximately one-third of human breast cancers are prolactin dependent *in vitro*, a factor of potential importance if the prescription of these drugs is contemplated in a patient with a previously detected breast cancer. Although disturbances such as galactorrhea, amenorrhea, gynecomastia, and impotence have been reported, the clinical significance of elevated serum prolactin levels is unknown for most patients. An increase in mammary neoplasms has been found in rodents after chronic administration of antipsychotic drugs. Neither clinical studies nor epidemiologic studies conducted to date, however, have shown an association between chronic administration of these drugs and mammary tumorigenesis: the available evidence is considered too limited to be conclusive at this time.

*Usage in Pregnancy:* Pregnancy Category C. Safe use in pregnancy or in women likely to become pregnant has not been established; use only if benefit clearly justifies potential hazards to the fetus.

*Nursing Mothers:* Infants should not be nursed during drug treatment.

*Pediatric Use:* Controlled trials to establish the safety and effectiveness of intramuscular administration in children have not been conducted.

**Adverse Reactions:** Adverse reactions following the administration of HALDOL Decanoate 50 or HALDOL Decanoate 100 are those of HALDOL haloperidol. Since vast experience has accumulated with HALDOL, the adverse reactions are reported for that compound as well as for haloperidol decanoate. As with all injectable medications, local tissue reactions have been reported with haloperidol decanoate.

*CNS Effects: Extrapyramidal Reactions*—Neuromuscular (extrapyramidal) reactions have been reported frequently, often during the first few days of treatment. Generally they involved Parkinson-like symptoms which when first observed were usually mild to moderately severe and usually reversible. Other types of neuromuscular reactions (motor restlessness, dystonia, akathisia, hyperreflexia, opisthotonos, oculogyric crises) have been reported far less frequently, but were often more severe. Severe extrapyramidal reactions have been reported at relatively low doses. Generally, extrapyramidal symptoms are dose-related since they occur at relatively high doses and disappear or become less severe when the dose is reduced. Antiparkinson drugs may be required. Persistent extrapyramidal reactions have been reported and the drug may have to be discontinued in such cases. *Withdrawal Emergent Neurological Signs*—Abrupt discontinuation of short-term antipsychotic therapy is generally uneventful. However, some patients on maintenance treatment experience transient dyskinetic signs after abrupt withdrawal. In certain cases these are indistinguishable from "Tardive Dyskinesia" except for duration. It is unknown whether gradual withdrawal will reduce the occurrence of these signs, but until further evidence is available HALDOL should be gradually withdrawn. *Tardive Dyskinesia*—As with all antipsychotic agents HALDOL has been associated with persistent dyskinesias. Tardive dyskinesia, a syndrome consisting of potentially irreversible, involuntary, dyskinetic movements, may appear in some patients on long-term therapy or may occur after drug therapy has been discontinued. The risk appears to be greater in elderly patients on high-dose therapy, especially females. The symptoms are persistent and in some patients irreversible. The syndrome is characterized by rhythmical involuntary movements of tongue, face, mouth or jaw (e.g., protrusion of tongue, puffing of cheeks, puckering of mouth, chewing movements). Sometimes these may be accompanied by involuntary movements of extremities and the trunk. There is no known effective treatment for tardive dyskinesia; antiparkinson agents usually do not alleviate the symptoms of this syndrome. It is suggested that all antipsychotic agents be discontinued if these symptoms appear. Should it be necessary to reinstitute treatment, or increase the dosage of the agent, or switch to a different antipsychotic agent, this syndrome may be masked. It has been reported that fine vermicular movement of the tongue may be an early sign of tardive dyskinesia and if the medication is stopped at that time the full syndrome may not develop. *Tardive Dystonia*—Tardive dystonia, not associated with the above syndrome, has also been reported. Tardive dystonia is characterized by delayed onset of choreic or dystonic movements, is often persistent, and has the potential of becoming irreversible. *Other CNS Effects*—Insomnia, restlessness, anxiety, euphoria, agitation, drowsiness, depression, lethargy, headache, confusion, vertigo, grand mal seizures, and exacerbation of psychotic symptoms including hallucinations, and catatonic-like behavioral states which may be responsive to drug withdrawal and/or treatment with anticholinergic drugs.

*Body as a Whole:* Neuroleptic malignant syndrome (NMS), hyperpyrexia and heat stroke have been reported with HALDOL. (See WARNINGS for further information concerning NMS.) *Cardiovascular Effects:* Tachycardia, hypotension, hypertension and ECG changes. *Hematologic Effects:* Reports of mild, usually transient leukopenia and leukocytosis, minimal decreases in red blood cell counts, anemia, or a tendency toward lymphomonocytosis; agranulocytosis rarely reported and only in association with other medication. *Liver Effects:* Impaired liver function and/or jaundice. *Dermatologic Reactions:* Maculopapular and acneiform reactions, isolated cases of photosensitivity, loss of hair. *Endocrine Disorders:* Lactation, breast engorgement, mastalgia, menstrual irregularities, gynecomastia, impotence, increased libido, hyperglycemia, hypoglycemia and hyponatremia. *Gastrointestinal Effects:* Anorexia, constipation, diarrhea, hypersalivation, dyspepsia, nausea and vomiting. *Autonomic Reactions:* Dry mouth, blurred vision, urinary retention, diaphoresis, and priapism. *Respiratory Effects:* Laryngospasm, bronchospasm and increased depth of respiration. *Special Senses:* Cataracts, retinopathy and visual disturbances. *Other:* Cases of sudden and unexpected death have been reported in association with the administration of HALDOL. The nature of the evidence makes it impossible to determine definitively what role, if any, HALDOL played in the outcome of the reported cases. The possibility that HALDOL caused death cannot, of course, be excluded, but it is to be kept in mind that sudden and unexpected death may occur in psychotic patients when they go untreated or when they are treated with other antipsychotic drugs.

**IMPORTANT: Full directions for use should be read before HALDOL or HALDOL Decanoate products are administered or prescribed.**

**For information on symptoms and treatment of overdosage, see full prescribing information.**

The short-acting HALDOL injectable form is intended only for acutely agitated psychotic patients with moderately severe to very severe symptoms.

McNeil Pharmaceutical, McNEILAB, INC., Spring House, PA 19477

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# THE AMERICAN JOURNAL OF PSYCHIATRY

Volume 147, Number 2 February 1990

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Systematic Comparison of Three Psychotherapies

By T. Byram Karasu

The Evolution of Systems of Mental Health Care:
The Arizona Experience

By Jose M. Santiago

Partial Hospitalization: An Update

By Susanna Parker and James L. Knoll III

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**References: 1.** Rickels K, et al. Buspirone and diazepam in anxiety: A controlled study. *J Clin Psychiatry* 1982;43(12, Sec 2):81-86. **2.** Newton RE, et al: A review of the side effect profile of buspirone. *Am J Med* 1986;80(suppl 3B):17-21. **3.** Lucki I, et al: Differential effects of the anxiolytic drugs, diazepam and buspirone, on memory function. *Br J Clin Pharmacol* 1987;23:207-211. **4.** Lader M: Assessing the potential for buspirone dependence or abuse and effects of its withdrawal. *Am J Med* 1987;82(suppl 5A):20-26.

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**Contraindications:** Hypersensitivity to buspirone hydrochloride.

**Warnings: The administration of BuSpar to a patient taking a monoamine oxidase inhibitor (MAOI) may pose a hazard.** Since blood pressure has become elevated when BuSpar was administered concomitantly with an MAOI, such concomitant use is not recommended. BuSpar should not be employed in lieu of appropriate antipsychotic treatment.

**Precautions: *General*—***Interference with cognitive and motor performance:* Although buspirone is less sedating than other anxiolytics and does not produce significant functional impairment, its CNS effects in a given patient may not be predictable; therefore, patients should be cautioned about operating an automobile or using complex machinery until they are reasonably certain that buspirone does not affect them adversely. Although buspirone has not been shown to increase alcohol-induced impairment in motor and mental performance, it is prudent to avoid concomitant use with alcohol.

*Potential for withdrawal reactions in sedative/hypnotic/anxiolytic drug dependent patients:* Because buspirone will not block the withdrawal syndrome often seen with cessation of therapy with benzodiazepines and other common sedative/hypnotic drugs, before starting buspirone withdraw patients gradually from their prior treatment, especially those who used a CNS depressant chronically. Rebound or withdrawal symptoms may occur over varying time periods, depending in part on the type of drug and its elimination half-life. The withdrawal syndrome can appear as any combination of irritability, anxiety, agitation, insomnia, tremor, abdominal cramps, muscle cramps, vomiting, sweating, flu-like symptoms without fever, and occasionally, even as seizures.

*Possible concerns related to buspirone's binding to dopamine receptors:* Because buspirone can bind to central dopamine receptors, a question has been raised about its potential to cause acute and chronic changes in dopamine mediated neurological function (eg, dystonia, pseudoparkinsonism, akathisia, and tardive dyskinesia). Clinical experience in controlled trials has failed to identify any significant neuroleptic-like activity; however, a syndrome of restlessness, appearing shortly after initiation of treatment, has been reported; the syndrome may be due to increased central noradrenergic activity or may be attributable to dopaminergic effects (ie, represent akathisia).

***Information for Patients*—**Patients should be instructed to inform their physician about any medications, prescription or nonprescription, alcohol or drugs they are now taking or plan to take during treatment with buspirone; to inform their physician if they are pregnant, are planning to become pregnant, or become pregnant while taking buspirone; to inform their physician if they are breast feeding; and not to drive a car or operate potentially dangerous machinery until they experience how this medication affects them.

***Drug Interactions*—**Concomitant use with other CNS active drugs should be approached with caution (see **Warnings**). Concomitant use with trazodone may have caused 3- to 6-fold elevations on SGPT (ALT) in a few patients. Concomitant administration of BuSpar and haloperidol resulted in increased serum haloperidol concentrations in normal volunteers. The clinical significance is not clear. Buspirone does not displace tightly bound drugs like phenytoin, propranolol, and warfarin from serum proteins, but may displace less firmly bound drugs like digoxin. However, there was one report of prolonged prothrombin time when buspirone was given to a patient also treated with warfarin, phenytoin, phenobarbital, digoxin, and Synthroid.

***Carcinogenesis, Mutagenesis, Impairment of Fertility*—**No evidence of carcinogenic potential was observed in rats or mice; buspirone did not induce point mutations, nor was DNA damage observed; chromosomal aberrations or abnormalities did not occur.

***Pregnancy: Teratogenic Effects*—**Pregnancy Category B: Should be used during pregnancy only if clearly needed.

***Nursing Mothers*—**Administration to nursing women should be avoided if clinically possible.

***Pediatric Use*—**The safety and effectiveness have not been determined in individuals below 18 years of age.

***Use in the Elderly*—**No unusual, adverse, age-related phenomena have been identified in elderly patients receiving a total, modal daily dose of 15 mg.

***Use in Patients with Impaired Hepatic or Renal Function*—**Since buspirone is metabolized by the liver and excreted by the kidneys, it is not recommended in severe hepatic or renal impairment.

**Adverse Reactions (See also Precautions): *Commonly Observed*—**The more commonly observed untoward events, not seen at an equivalent incidence in placebo-treated patients, include dizziness, nausea, headache, nervousness, lightheadedness, and excitement.

***Associated with Discontinuation of Treatment*—**The more common events causing discontinuation in-

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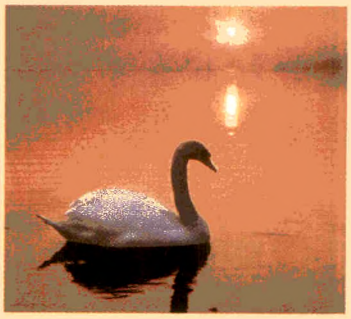

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The more commonly observed untoward events associated with the use of BuSpar not seen at an equivalent incidence among placebo-treated patients include dizziness (12%), nausea (8%), headache (6%), nervousness (5%), lightheadedness (3%), and excitement (2%).

*Because the effects of BuSpar in any individual patient may not be predictable, patients should be cautioned about operating an automobile or using complex machinery until they are reasonably certain that BuSpar treatment does not affect them adversely.

ed: central nervous system disturbances (3 4%). primarily dizziness, insomnia, nervousness, drowsiness,
eaded feeling; gastrointestinal disturbances (1.2%), primarily nausea; miscellaneous disturbances
), primarily headache and fatigue. In addition, 3.4% of patients had multiple complaints, none of which
 be characterized as primary.

***lence in Controlled Clinical Trials***—Adverse events reported by 1% or more of 477 patients who re-
d buspirone in four-week, controlled trials: *Cardiovascular:* Tachycardia/palpitations 1%. *CNS:* Dizziness
drowsiness 10%, nervousness 5%, insomnia 3%, lightheadedness 3%, decreased concentration 2%,
ement 2%, anger/hostility 2%, confusion 2%, depression 2%. *EENT:* Blurred vision 2%. *Gastrointestinal:*
ea 8%, dry mouth 3%, abdominal/gastric distress 2%, diarrhea 2%, constipation 1%, vomiting 1%. *Mus-
keletal:* Musculoskeletal aches/pains 1%. *Neurological:* Numbness 2%, paresthesia 1%, incoordination
remor 1%. *Skin:* Skin rash 1%. *Miscellaneous:* Headache 6%, fatigue 4%, weakness 2%, sweating/
miness 1%.

***r Events Observed During the Entire Premarketing Evaluation***—The relative frequency of all
undesirable events reasonably associated with the use of buspirone in approximately 3000 subjects who
nultiple doses of the drug under well-controlled, open, and uncontrolled conditions is defined as follows:
ent are those occurring in at least 1/100 patients; infrequent are those occurring in 1/100 to 1/1000 patients;
are are those occurring in less than 1/1000 patients. *Cardiovascular*—frequent: non-specific chest pain; in-
ent: syncope, hypotension, hypertension, rare: cerebrovascular accident, congestive heart failure, myo-
al infarction, cardiomyopathy, bradycardia. *Central Nervous System*—frequent: dream disturbances;
uent: depersonalization, dysphoria, noise intolerance, euphoria, akathisia, fearfulness, loss of interest,
ciative reaction, hallucinations, suicidal ideation, seizures; rare: feelings of claustrophobia, cold intoler-
stupor, slurred speech, psychosis. *EENT*—frequent: tinnitus, sore throat, nasal congestion; infrequent:
ss and itching of the eyes, altered taste, altered smell, conjunctivitis; rare: inner ear abnormality, eye pain,
phobia, pressure on eyes. *Endocrine*—rare: galactorrhea, thyroid abnormality. *Gastrointestinal*—
uent: flatulence, anorexia, increased appetite, salivation, irritable colon, rectal bleeding; rare: burning of
ngue. *Genitourinary*—infrequent: urinary frequency, urinary hesitancy, menstrual irregularity and spot-
dysuria; rare: amenorrhea, pelvic inflammatory disease, enuresis, nocturia. *Musculoskeletal*—infrequent:
le cramps, muscle spasms, rigid/stiff muscles, arthralgias. *Neurological*—infrequent: involuntary move-
, slowed reaction time; rare: muscle weakness. *Respiratory*—infrequent: hyperventilation, shortness of breath, chest congestion; rare: epistaxis. *Sexual Function*—infrequent: decreased or increased libido; rare: delayed ejaculation, impotence. *Skin*—infrequent: edema, pruritus, flushing, easy bruising, hair loss, dry skin, facial edema, blisters; rare: acne, thinning of nails. *Clinical Laboratory*—infrequent: increases in hepatic aminotransferases (SGOT, SGPT); rare: eosinophilia, leukopenia, thrombocytopenia. *Miscellaneous*—infrequent: weight gain, fever, roaring sensation in the head, weight loss, malaise; rare: alcohol abuse, bleeding disturbance, loss of voice, hiccoughs.

***Postintroduction Clinical Experience***—Rare occurrences of allergic reactions, cogwheel rigidity, dystonic reactions, ecchymosis, emotional lability, tunnel vision, and urinary retention have been reported. Because of the uncontrolled nature of these spontaneous reports, a causal relationship to BuSpar has not been determined.

**Drug Abuse and Dependence: *Controlled Substance Class***—Not a controlled substance.

***Physical and Psychological Dependence***—Buspirone has shown no potential for abuse or diversion and there is no evidence that it causes tolerance, or either physical or psychological dependence. However, since it is difficult to predict from experiments the extent to which a CNS-active drug will be misused, diverted, and/or abused once marketed, physicians should carefully evaluate patients for a history of drug abuse and follow such patients closely, observing them for signs of buspirone misuse or abuse (eg, development of tolerance, incrementation of dose, drug-seeking behavior).

**Overdosage: *Signs and Symptoms***—At doses approaching 375 mg/day the following symptoms were observed: nausea, vomiting, dizziness, drowsiness, miosis, and gastric distress. No deaths have been reported in humans either with deliberate or accidental overdosage.

***Recommended Overdose Treatment***—General symptomatic and supportive measures should be used along with immediate gastric lavage. No specific antidote is known and dialyzability of buspirone has not been determined.

*For complete details, see Prescribing Information or consult your Mead Johnson Pharmaceuticals Representative.*

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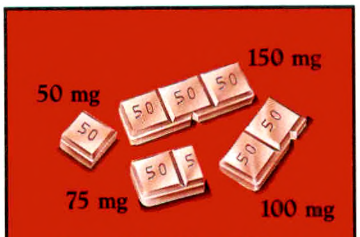

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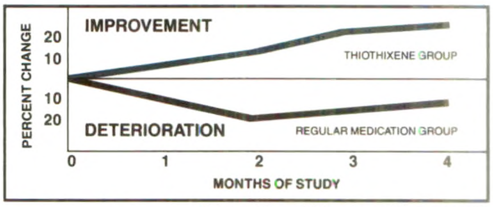
# "IT FEELS GOOD TO FEEL USEFUL AGAIN"

For the chronic schizophrenic patient, Navane can mean more competent work performance,[1,2] and a smoother path towards social recovery. Navane may help improve the ability to concentrate, and promote a better attitude toward work and co-workers.[1-3]

Anticholinergic[4] and cardiovascular[5,6] side effects in patients treated with Navane are reported infrequently. Should extrapyramidal symptoms occur, they usually can be controlled.

**27% rise in work output compared to baseline shown in patients switched to Navane[2,3]**



(Adapted from DiMascio and Demirgian[2,3])

Forty-two psychotic male and female patients under age 55 were entered in this study on a nonblind basis, and randomly assigned to their regular medication or switched to thiothixene. Patients were evaluated at baseline and on a daily basis, and periodically rated on the Global Improvement and Brief Psychiatric Rating Scales.

**In schizophrenia,**

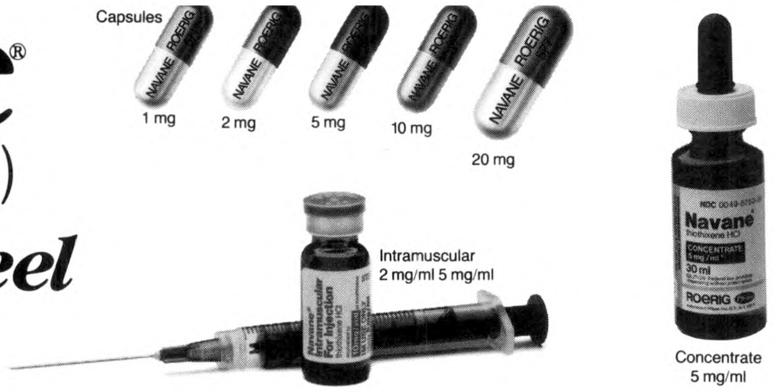
**Navane®** (thiothixene) (thiothixene HCl)

Please see brief summary of NAVANE® (thiothixene/thiothixene HCl) prescribing information on adjacent page.

# Navane®

## (thiothixene) (thiothixene HCl)

## *It feels good to feel useful again*



**References:** 1. Bressler B, Friedel RO: A comparison between chlorpromazine and thiothixene in a Veterans Administration hospital population. *Psychosomatics* 1971;12:275-277. 2. DiMascio A, Demirgian E: Study of the activating properties of thiothixene. *Psychosomatics* 1972;13:105-108. 3. DiMascio A, Demirgian E: Job training in the rehabilitation of the chronic schizophrenic. Presented as a Scientific Exhibit at The American Psychiatric Association. Washington, DC, May 3-6, 1971. 4. Goldstein B, Weiner D, Banas F: Clinical evaluation of thiothixene in chronic ambulatory schizophrenic patients, in Lehmann HE, Ban TA (eds): *The Thioxanthenes: Modern Problems of Pharmacopsychiatry.* Basel, Switzerland, S. Karger, 1969, vol 2, pp 45-52. 5. Dillenkoffer RL, Gallant DM, George RB, et al: Electrocardiographic evaluation of schizophrenic patients: A double-blind comparison. Presented as a Scientific Exhibit at The 125th Annual Meeting of the American Psychiatric Association, Dallas, May 1-4, 1972. 6. Data available on request from Roerig.

**BRIEF SUMMARY OF PRESCRIBING INFORMATION**
**Navane® (thiothixene) Capsules: 1 mg, 2 mg, 5 mg, 10 mg, 20 mg**
**(thiothixene hydrochloride) Concentrate: 5 mg/ml, Intramuscular: 2 mg/ml, 5 mg/ml**

**Indications:** Navane is effective in the management of manifestations of psychotic disorders. Navane has not been evaluated in the management of behavioral complications in patients with mental retardation.

**Contraindications:** Contraindicated in patients with circulatory collapse, comatose states, central nervous system depression due to any cause, and blood dyscrasias. Contraindicated in individuals who have shown hypersensitivity to the drug. It is not known whether there is a cross-sensitivity between the thioxanthenes and the phenothiazine derivatives, but the possibility should be considered.

**Warnings:** *Tardive Dyskinesia*—Tardive dyskinesia, a syndrome consisting of potentially irreversible, involuntary, dyskinetic movements may develop in patients treated with neuroleptic (antipsychotic) drugs. Although the prevalence of the syndrome appears to be highest among the elderly, especially elderly women, it is impossible to rely upon prevalence estimates to predict, at the inception of neuroleptic treatment, which patients are likely to develop the syndrome. Whether neuroleptic drug products differ in their potential to cause tardive dyskinesia is unknown.

Both the risk of developing the syndrome and the likelihood that it will become irreversible are believed to increase as the duration of treatment and the total cumulative dose of neuroleptic drugs administered to the patient increase. However, the syndrome can develop, although much less commonly, after relatively brief treatment periods at low doses.

There is no known treatment for established cases of tardive dyskinesia, although the syndrome may remit, partially or completely, if neuroleptic treatment is withdrawn. Neuroleptic treatment, itself, however, may suppress (or partially suppress) the signs and symptoms of the syndrome and thereby may possibly mask the underlying disease process. The effect that symptomatic suppression has upon the long-term course of the syndrome is unknown.

Given these considerations, neuroleptics should be prescribed in a manner that is most likely to minimize the occurrence of tardive dyskinesia. Chronic neuroleptic treatment should generally be reserved for patients who suffer from a chronic illness that, 1) is known to respond to neuroleptic drugs, and, 2) for whom alternative, equally effective, but potentially less harmful treatments are *not* available or appropriate. In patients who do require chronic treatment, the smallest dose and the shortest duration of treatment producing a satisfactory clinical response should be sought. The need for continued treatment should be reassessed periodically.

If signs and symptoms of tardive dyskinesia appear in a patient on neuroleptics, drug discontinuation should be considered. However, some patients may require treatment despite the presence of the syndrome.

(For further information about the description of tardive dyskinesia and its clinical detection, please refer to Information for Patients in the Precautions section, and to the Adverse Reactions section.)

*Neuroleptic Malignant Syndrome (NMS)*—A potentially fatal symptom complex sometimes referred to as Neuroleptic Malignant Syndrome (NMS) has been reported in association with antipsychotic drugs. Clinical manifestations of NMS are hyperpyrexia, muscle rigidity, altered mental status and evidence of autonomic instability (irregular pulse or blood pressure, tachycardia, diaphoresis, and cardiac dysrhythimas).

The diagnostic evaluation of patients with this syndrome is complicated. In arriving at a diagnosis, it is important to identify cases where the clinical presentation includes both serious medical illness (e.g., pneumonia, systemic infection, etc.) and untreated or inadequately treated extrapyramidal signs and symptoms (EPS). Other important considerations in the differential diagnosis include central anticholinergic toxicity, heat stroke, drug fever and primary central nervous system (CNS) pathology.

The management of NMS should include 1) immediate discontinuation of antipsychotic drugs and other drugs not essential to concurrent therapy, 2) intensive symptomatic treatment and medical monitoring, and 3) treatment of any concomitant serious medical problems for which specific treatments are available. There is no general agreement about specific pharmacological treatment regimens for uncomplicated NMS.

If a patient requires antipsychotic drug treatment after recovery from NMS, the potential reintroduction of drug therapy should be carefully considered. The patient should be carefully monitored, since recurrences of NMS have been reported.

*Usage in Pregnancy*—Safe use of Navane during pregnancy has not been established. Therefore, this drug should be given to pregnant patients only when, in the judgment of the physician, the expected benefits from the treatment exceed the possible risks to mother and fetus. Animal reproduction studies and clinical experience to date have not demonstrated any teratogenic effects.

In the animal reproduction studies with Navane, there was some decrease in conception rate and litter size, and an increase in resorption rate in rats and rabbits, changes which have been similarly reported with other psychotropic agents. After repeated oral administration of Navane to rats (5 to 15 mg/kg/day), rabbits (3 to 50 mg/kg/day), and monkeys (1 to 3 mg/kg/day) before and during gestation, no teratogenic effects were seen. (See Precautions.)

*Usage in Children*—The use of Navane in children under 12 years of age is not recommended because safety and efficacy in the pediatric age group have not been established.

As is true with many CNS drugs, Navane may impair the mental and/or physical abilities required for the performance of potentially hazardous tasks such as driving a car or operating machinery, especially during the first few days of therapy. Therefore, the patient should be cautioned accordingly.

As in the case of other CNS-acting drugs, patients receiving Navane should be cautioned about the possible additive effects (which may include hypotension) with CNS depressants and with alcohol.

**Precautions:** An antiemetic effect was observed in animal studies with Navane; since this effect may also occur in man, it is possible that Navane may mask signs of overdosage of toxic drugs and may obscure conditions such as intestinal obstruction and brain tumor.

In consideration of the known capability of Navane and certain other psychotropic drugs to precipitate convulsions, extreme caution should be used in patients with a history of convulsive disorders or those in a state of alcohol withdrawal since it may lower the convulsive threshold. Although Navane potentiates the actions of the barbiturates, the dosage of the anticonvulsant therapy should not be reduced when Navane is administered concurrently.

Caution as well as careful adjustment of the dosage is indicated when Navane is used in conjunction with other CNS depressants other than anticonvulsant drugs.

Though exhibiting rather weak anticholinergic properties, Navane should be used with caution in patients who are known or suspected to have glaucoma, or who might be exposed to extreme heat, or who are receiving atropine or related drugs.

Use with caution in patients with cardiovascular disease.

Also, careful observation should be made for pigmentary retinopathy, and lenticular pigmentation (fine lenticular pigmentation has been noted in a small number of patients treated with Navane for prolonged periods). Blood dyscrasias (agranulocytosis, pancytopenia, thrombocytopenic purpura), and liver damage (jaundice, biliary stasis) have been reported with related drugs.

Undue exposure to sunlight should be avoided. Photosensitive reactions have been reported in patients on Navane (thiothixene).

*Intramuscular Administration*—As with all intramuscular preparations, Navane Intramuscular should be injected well within the body of a relatively large muscle. The preferred sites are the upper outer quadrant of the buttock (i.e. gluteus maximus) and the mid-lateral thigh.

The deltoid area should be used only if well developed, such as in certain adults and older children, and then only with caution to avoid radial nerve injury. Intramuscular injections should not be made into the lower and mid-thirds of the upper arm. As with all intramuscular injections, aspiration is necessary to help avoid inadvertent injection into a blood vessel.

Neuroleptic drugs elevate prolactin levels; the elevation persists during chronic administration. Tissue culture experiments indicate that approximately one third of human breast cancers are prolactin-dependent *in vitro*, a factor of potential importance if the prescription of these drugs is contemplated in a patient with a previously detected breast cancer. Although disturbances such as galactorrhea, amenorrhea, gynecomastia, and impotence have been reported, the clinical significance of elevated serum prolactin levels is unknown for most patients. An increase in mammary neoplasms has been found in rodents after chronic administration of neuroleptic drugs. Neither clinical studies nor epidemiologic studies conducted to date, however, have shown an association between chronic administration of these drugs and mammary tumorigenesis; the available evidence is considered too limited to be conclusive at this time.

*Information for Patients*—Given the likelihood that some patients exposed chronically to neuroleptics will develop tardive dyskinesia, it is advised that all patients in whom chronic use is contemplated be given, if possible, full information about this risk. The decision to inform patients and/or their guardians must obviously take into account the clinical circumstances and the competency of the patient to understand the information provided.

**Adverse Reactions:** *Note:* Not all of the following adverse reactions have been reported with Navane (thiothixene). However, since Navane has certain chemical and pharmacologic similarities to the phenothiazines, all of the known side effects and toxicity associated with phenothiazine therapy should be borne in mind when Navane is used.

Cardiovascular effects: Tachycardia, hypotension, lightheadedness, and syncope. In the event hypotension occurs, epinephrine should not be used as a pressor agent since a paradoxical further lowering of blood pressure may result. Nonspecific EKG changes have been observed in some patients receiving Navane (thiothixene). These changes are usually reversible and frequently disappear on continued Navane therapy. The incidence of these changes is lower than that observed with some phenothiazines. The clinical significance of these changes is not known.

CNS effects: Drowsiness, usually mild, may occur although it usually subsides with continuation of Navane therapy. The incidence of sedation appears similar to that of the piperazine group of phenothiazines, but less than that of certain aliphatic phenothiazines. Restlessness, agitation and insomnia have been noted with Navane. Seizures and paradoxical exacerbation of psychotic symptoms have occurred with Navane infrequently.

Hyperreflexia has been reported in infants delivered from mothers having received structurally related drugs.

In addition, phenothiazine derivatives have been associated with cerebral edema and cerebrospinal fluid abnormalities.

Extrapyramidal symptoms, such as pseudo-parkinsonism, akathisia, and dystonia have been reported. Management of these extrapyramidal symptoms depends upon the type and severity. Rapid relief of acute symptoms may require the use of an injectable antiparkinson agent. More slowly emerging symptoms may be managed by reducing the dosage of Navane and/or administering an oral antiparkinson agent.

Persistent Tardive Dyskinesia: As with all antipsychotic agents tardive dyskinesia may appear in some patients on long-term therapy or may occur after drug therapy has been discontinued. The syndrome is characterized by rhythmical involuntary movements of the tongue, face, mouth or jaw (e.g., protrusion of tongue, puffing of cheeks, puckering of mouth, chewing movements). Sometimes these may be accompanied by involuntary movements of extremities.

Since early detection of tardive dyskinesia is important, patients should be monitored on an ongoing basis. It has been reported that fine vermicular movement of the tongue may be an early sign of the syndrome. If this or any other presentation of the syndrome is observed, the clinician should consider possible discontinuation of neuroleptic medication. (See Warnings section.)

Hepatic Effects: Elevations of serum transaminase and alkaline phosphatase, usually transient, have been infrequently observed in some patients. No clinically confirmed cases of jaundice attributable to Navane have been reported.

Hematologic Effects: As is true with certain other psychotropic drugs, leukopenia and leukocytosis, which are usually transient, can occur occasionally with Navane. Other antipsychotic drugs have been associated with agranulocytosis, eosinophilia, hemolytic anemia, thrombocytopenia and pancytopenia.

Allergic Reactions: Rash, pruritus, urticaria, photosensitivity and rare cases of anaphylaxis have been reported with Navane. Undue exposure to sunlight should be avoided. Although not experienced with Navane, exfoliative dermatitis and contact dermatitis (in nursing personnel) have been reported with certain phenothiazines.

Endocrine Disorders: Lactation, moderate breast enlargement and amenorrhea have occurred in a small percentage of females receiving Navane. If persistent, this may necessitate a reduction in dosage or the discontinuation of therapy. Phenothiazines have been associated with false positive pregnancy tests, gynecomastia, hypoglycemia, hyperglycemia, and glycosuria.

Autonomic Effects: Dry mouth, blurred vision, nasal congestion, constipation, increased sweating, increased salivation, and impotence have occurred infrequently with Navane therapy. Phenothiazines have been associated with miosis, mydriasis, and adynamic ileus.

Other Adverse Reactions: Hyperpyrexia, anorexia, nausea, vomiting, diarrhea, increase in appetite and weight, weakness or fatigue, polydipsia and peripheral edema.

Although not reported with Navane, evidence indicates there is a relationship between phenothiazine therapy and the occurrence of a systemic lupus erythematosus-like syndrome.

*Neuroleptic Malignant Syndrome (NMS): Please refer to the text regarding NMS in the WARNINGS section.*

NOTE: Sudden deaths have occasionally been reported in patients who have received certain phenothiazine derivatives. In some cases the cause of death was apparently cardiac arrest or asphyxia due to failure of the cough reflex. In others, the cause could not be determined nor could it be established that death was due to phenothiazine administration.

**Dosage:** Dosage of Navane should be individually adjusted depending on the chronicity and severity of the condition. See full prescribing information.

**Overdosage:** For information on signs and symptoms, and treatment of overdosage, see full prescribing information.

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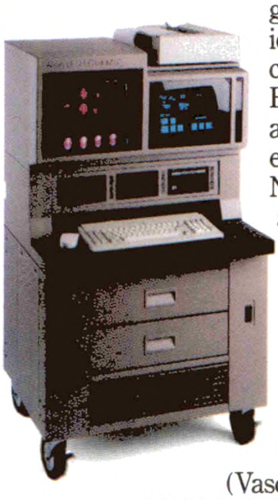

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# Calendar

*For free listing of your organization's official annual or regional meeting, please send us the following information: sponsor, location, inclusive dates, type and number of continuing education credits (if available), and the name, address, and telephone number of the person or group to contact for more information. All notices and changes must be received no later than 120 days before the first day of the month of desired publication and should be addressed to Calendar,* American Journal of Psychiatry, *1400 K St., N.W., Washington, DC 20005. Because of space limitations, only listings of meetings of the greatest interest to* Journal *readers will be included.*

## APRIL

April 1–6, 6th World Congress on Pain, Norwood, South Australia. Contact Elliservice Convention Management, P.O. Box 753, Norwood, South Australia 5067; 08-332-4068 or 08-31-5687.

April 4–6, International Symposium on New Concepts in Anxiety, Castres, France. Contact Martine Dehaye, Centre de Recherche Pierre Fabre, 17 avenue Jean Moulin, 81100 Castres, France; 63-35-56-07.

April 4–6, annual meeting, Group for the Advancement of Psychiatry, White Plains, New York. Contact Carolyn Robinowitz, M.D., President, 1400 K Street, NW, Washington, DC 20005; 202-682-6331.

April 6–8, annual meeting, Association for Child Psychoanalysis, Santa Fe, New Mexico. Contact Robert D. Gillman, M.D., President, P.O. Box 5935, Washington, DC 20016; 202-363-7849.

April 11–14, Asian Medicine: Past, Present and Future (Mental Health Care and Methods, Use of Medicinal Plants, Concepts and Applications of Acupuncture, and Other Alternative General Medical Practices), Bangkok, Thailand. Contact Ann McCormick, Southern California Neuropsychiatric Institute, 6794 La Jolla Blvd, La Jolla, CA 92037; 619-454-2102.

April 12–14, annual meeting, Bulimia Anorexia Self-Help, Inc., St. Louis. Contact Felix E.F. Larocca, M.D., President, 6125 Clayton Avenue, Suite 215, St. Louis, MO 63139; 314-567-4080.

April 18–21, annual meeting, Society of Behavioral Medicine, Chicago. Contact Judith C. Woodward, Executive Director, P.O. Box 8530, Knoxville, TN 37996; 615-974-5164.

April 19–21, 31st National Student Research Forum, University of Texas Medical Branch, Galveston, Texas. Contact National Student Research Forum, Room 209, Family Medicine Building, Route H-56, University of Texas Medical Branch, Galveston, TX 77550; 409-761-3762.

April 22–May 5, 2nd International Colloquium on Advances in Intensive Psychotherapy, Jerusalem. Contact David Fogel, M.D., 200 Fisher Building, Detroit, MI 48202.

April 24–27, 36th Annual Meeting of the American Society for Artificial Internal Organs, Washington, DC. Contact ASAIO, P.O. Box C, Boca Raton, FL 33429; 407-391-8589.

April 25–27, 1st International Congress of Movement Disorders, Washington, D.C. Contact Mark Hallett, M.D., Scientific Secretariat, National Institute of Neurologic Disorders and Stroke, National Institutes of Health, Building 10, Room 5N226, Bethesda, MD 20892; or Secretariat ISMD, P.O. Box CH-4005, Basel, Switzerland.

April 25–29, annual meeting, American Association of Suicidology, New Orleans. Contact Julie Perlman, M.S.W., Executive Officer, 2459 South Ash, Denver, CO 80222; 303-692-0985.

April 25–29, annual meeting, American Orthopsychiatric Association, Miami. Contact Herbert A. Sohn, Ph.D., Executive Director, 19 West 44th Street, Suite 1616, New York, NY 10036; 212-354-5770.

April 26–29, annual meeting, American College of Physicians, Chicago. Contact John Ball, M.D., J.D., Executive Vice-President, Independence Mall West, Philadelphia, PA 19106-1572; 215-351-2400.

April 26–29, annual meeting, National Council on Alcoholism, Inc., Phoenix, Arizona. Contact Hamilton Beazley, President, 12 West 21st Street, 8th Floor, New York, NY 10010; 212-206-6770.

April 27–29, 4th International Conference on Eating Disorders, New York. Contact Eric Schwartz, Program Administrator, Office of Continuing Medical Education, Albert Einstein College of Medicine/Montefiore Medical Center, 3301 Bainbridge Avenue, Bronx, New York 10467; 212-920-6674.

April 27–May 2, annual meeting, American Occupational Therapy Association, New Orleans. Contact Jeanette Bair, 1383 Piccard Drive, Rockville, MD 20850; 301-948-9626.

April 28—May 4, annual meeting, American College of Occupational Medicine, Houston. Contact Donald L. Hoops, Ph.D., Executive Director, 55 West Seegers Road, Arlington Heights, IL 60005; 312-228-6850.

*(Continued on page A34)*

# Productive Days... Restful Nights and Pamelor® (nortriptyline HCl)

## The Full-Time Antidepressant

### for patients whose symptoms include insomnia and anxiety

# PAMELOR®
# (nortriptyline HCl)

CAPSULES: 10 mg, 25 mg, 50 mg, and 75 mg; SOLUTION: 10 mg/5 mL and alcohol 4%

*The active metabolite of amitriptyline*

**Contraindications:** 1) Concurrent use w [illegible]
(MAO) inhibitor, since hyperpyretic crises, se [illegible]
talities have occurred when similar tricyclic a [illegible]
in such combinations. MAO inhibitors shou [illegible]
least two weeks before treatment with Pame [illegible]
started. 2) Hypersensitivity to Pamelor [illegible]
sensitivity with other dibenzazepines is a p [illegible]
ery period after myocardial infarction.
**Warnings:** Give only under close supervisi [illegible]
vascular disease, because of the tendency of [illegible]
tachycardia and to prolong conduction time. [illegible]
rhythmia, and strokes have occurred. The a [illegible]
guanethidine and similar agents may be blo [illegible]
cholinergic activity, nortriptyline should be [illegible]
patients who have glaucoma or a history of [illegible]
with a history of seizures should be followed [illegible]
is known to lower the convulsive threshold. G [illegible]
perthyroid patients or those receiving thyroid [illegible]
arrhythmias may develop. Nortriptyline may [illegible]
physical abilities required for the performance [illegible]
as operating machinery or driving a car; there [illegible]
warned accordingly. Excessive consumption [illegible]
tentiating effect, which may lead to the dange [illegible]
tempts or overdosage, especially in patients w [illegible]
disturbances or suicidal ideation.
The concomitant administration of quinidi [illegible]
result in a significantly longer plasma half-li [illegible]
clearance of nortriptyline.
*Use in Pregnancy* Safe use during pregnan [illegible]
been established; therefore, in pregnant pati [illegible]
women of childbearing potential, the potential [illegible]
against the possible hazards.
*Use in Children* -Not recommended for use [illegible]
and effectiveness in the pediatric age group h [illegible]
**Precautions:** Use in schizophrenic patients [illegible]
bation of the psychosis or may activate latent [illegible]
in overactive or agitated patients, increased a [illegible]
occur; in manic-depressive patients, symptom [illegible]
emerge. Administration of reserpine during th [illegible]
depressant has been shown to produce a "st [illegible]
depressed patients. Troublesome patient host [illegible]
leptiform seizures may accompany administr [illegible]
and careful adjustment of dosage are required w [illegible]
ticholinergic drugs and sympathomimetic dru [illegible]
tration of cimetidine can produce clinically si [illegible]
plasma concentrations of the tricyclic antide [illegible]
be informed that the response to alcohol may [illegible]
sential, may be administered with electrocon [illegible]
the hazards may be increased. Discontinue th [illegible]
possible, prior to elective surgery. The possib [illegible]
by a depressed patient remains after the initia [illegible]
regard, it is important that the least possible [illegible]
pensed at any given time. Both elevation and [illegible]
levels have been reported.
A case of significant hypoglycemia has been [illegible]
betic patient maintained on chlorpropamide ( [illegible]
dition of nortriptyline (125 mg/day).
**Adverse Reactions:** *Cardiovascular* - Hyp [illegible]
tachycardia, palpitation, myocardial infarct [illegible]
block, stroke. *Psychiatric* - Confusional stat [illegible]
derly) with hallucinations, disorientation, del [illegible]
ness, agitation, insomnia, panic, nightmares, [illegible]
of psychosis. *Neurologic* - Numbness, tingl [illegible]
tremities; incoordination, ataxia, tremors, peri [illegible]
pyramidal symptoms, seizures, alteration i [illegible]
*Anticholinergic* - Dry mouth and rarely asso [illegible]
tis; blurred vision, disturbance of accommod [illegible]
pation, paralytic ileus, urinary retention, delay [illegible]
the urinary tract. *Allergic* - Skin rash, petechia [illegible]
tosensitization (avoid excessive exposure to s [illegible]
or of face and tongue), drug fever, cross-sens [illegible]
drugs. *Hematologic* - Bone marrow depressio [illegible]
tosis; eosinophilia, purpura, thrombocytop [illegible]
Nausea and vomiting, anorexia, epigastric dis [illegible]
taste, stomatitis, abdominal cramps, blac [illegible]
Gynecomastia in the male, breast enlargemen [illegible]
female; increased or decreased libido, impote [illegible]
elevation or depression of blood sugar levels, [illegible]
ate ADH (antidiuretic hormone) secretion. *Oth* [illegible]
obstructive), altered liver function; weight ga [illegible]
flushing; urinary frequency, nocturia; drowsin [illegible]
fatigue, headache; parotid swelling, alopecia [illegible]
Though these are not indicative of addiction [illegible]
ment after prolonged therapy may produce [illegible]
malaise.
**Overdosage:** Toxic overdosage may result in [illegible]
agitation, vomiting, hyperpyrexia, muscle rigid [illegible]
tachycardia, ECG evidence of impaired condu [illegible]
heart failure, stupor, coma, and CNS stimulati [illegible]
lowed by respiratory depression. Deaths have [illegible]
this class. No specific antidote is known. Gen [illegible]
are indicated, with gastric lavage [illegible]

**SANDOZ** PHARMACEUTICALS
Corporation E. Hanover, [illegible]

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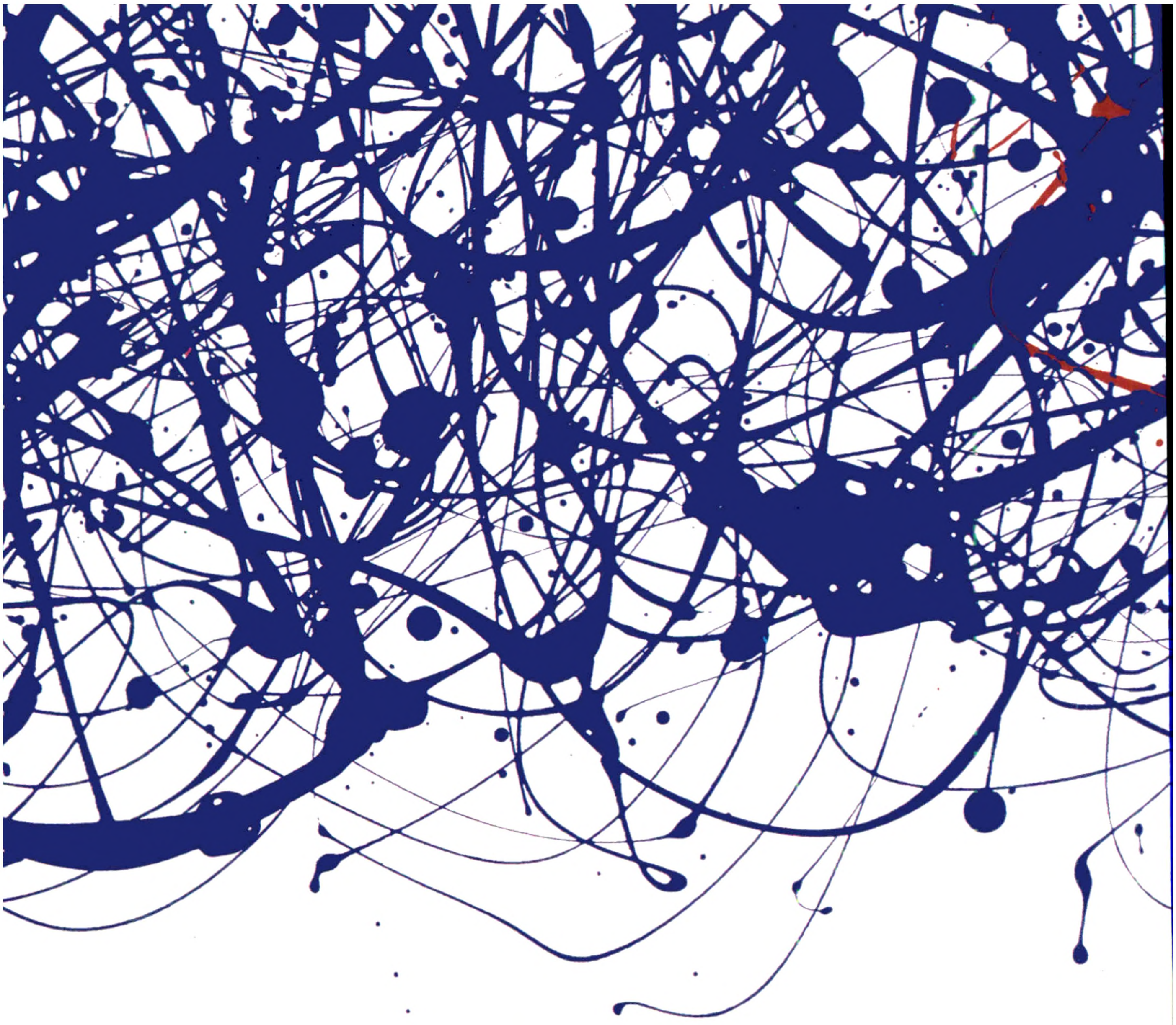
PAM-0789-04-D



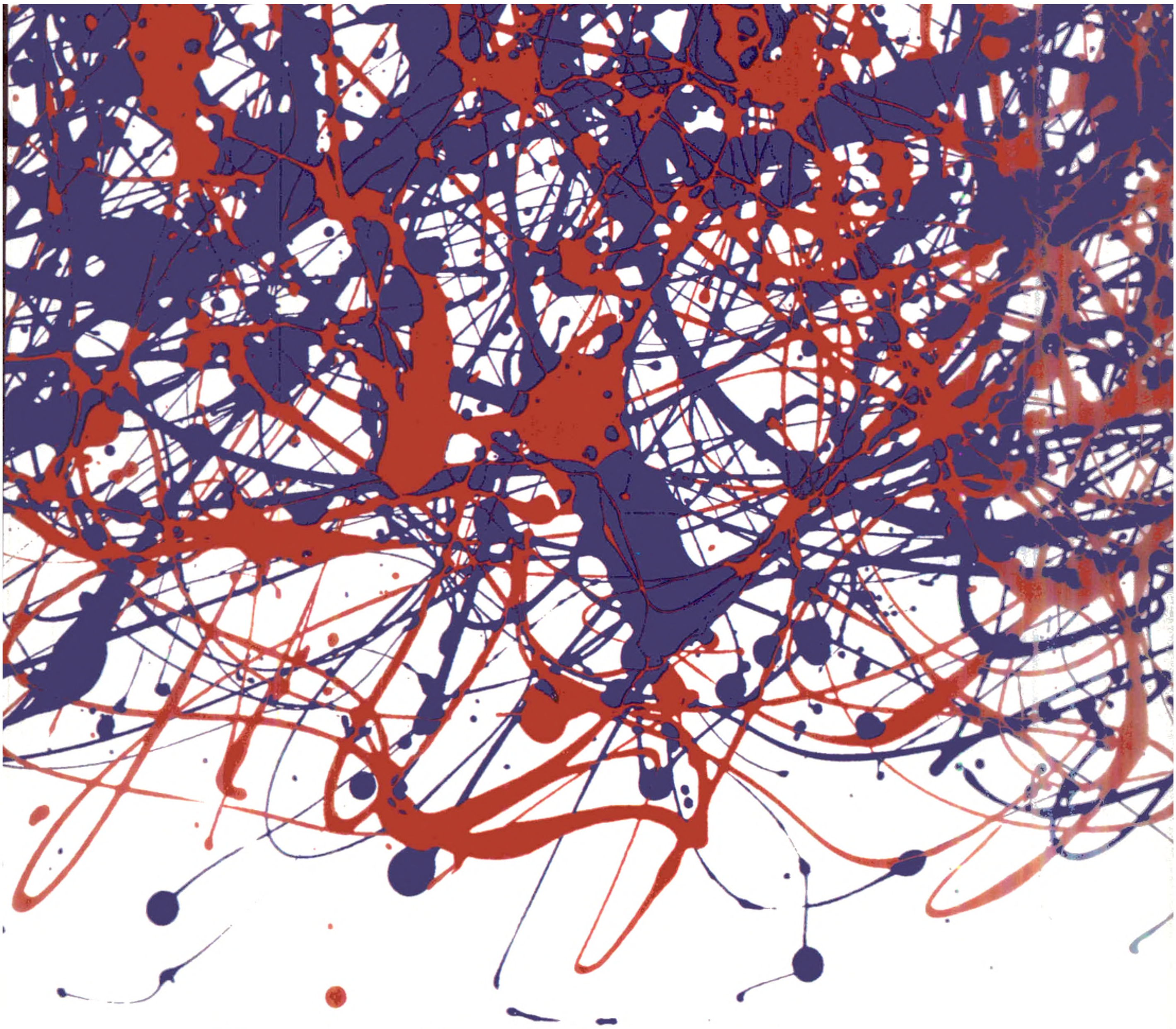
# With depression . .

In a clinical trial, XANAX was effective in reducing anxiety symptoms associated with moderate to severe depression.*

Patients taking XANAX should be alerted to possible additive CNS depressant effects when it is administered with other medications that produce CNS depression.

The usual starting dosage of XANAX is 0.25 to 0.5 mg t.i.d.

*Data on file, The Upjohn Company



ou often find anxiety

TABLETS 0.5 MG

**Xanax**®

alprazolam Ⓘⓥ

**For anxiety associated with depression**

**Upjohn** Please see adjacent page for brief summary of prescribing information.

The Upjohn Company
Kalamazoo, Michigan 49001, USA

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**XANAX® Tablets**
**(alprazolam, ©)**

**INDICATIONS AND USAGE**

Anxiety disorders, short-term relief of the symptoms of anxiety, and anxiety associated with depression. Anxiety or tension associated with the stress of everyday life usually does not require an anxiolytic. Effectiveness for more than four months has not been established; periodically reassess the usefulness of the drug for the individual patient.

**CONTRAINDICATIONS**

Sensitivity to XANAX or other benzodiazepines, and in acute narrow angle glaucoma

**WARNINGS**

XANAX is not of value in treating psychosis and should not be used in lieu of appropriate treatment. Patients receiving XANAX should be cautioned about hazardous occupations or activities requiring full alertness and also about simultaneous ingestion of alcohol or other CNS depressants.

Benzodiazepines can cause fetal harm in pregnant women, hence women who may become pregnant should be warned. Avoid during the first trimester. Withdrawal seizures have been reported upon rapid dose reduction or abrupt discontinuation, thus reduce dose gradually. (See Drug Abuse and Dependence and Dosage and Administration.)

**PRECAUTIONS**

***General*:** If XANAX is combined with other psychotropics or anticonvulsants, consider drug potentiation. (See Drug Interactions.) Use the usual precautions in patients with renal or hepatic impairment and regarding prescription size in depressed and suicidal patients. In elderly and debilitated patients, use the lowest possible dose. (See Dosage and Administration.) Hypomania and mania has been reported in depressed patients.

***Information for Patients*:** Alert patients about: (a) consumption of alcohol and drugs, (b) possible fetal abnormalities, (c) operating machinery or driving, (d) not increasing dose of the drug due to risk of dependence, (e) not stopping the drug abruptly. *Laboratory Tests*: Not ordinarily required in otherwise healthy patients. *Drug Interactions*: Additive CNS depressant effects with other psychotropics, anticonvulsants, antihistamines, ethanol and other CNS depressants. Plasma levels of imipramine and desipramine are increased. Pharmacokinetic interactions with other drugs have been reported. Cimetidine can delay clearance of benzodiazepines. *Drug/Laboratory Test Interactions*: No consistent pattern for a drug or test. *Carcinogenesis, Mutagenesis, Impairment of Fertility*: No carcinogenic potential or impairment of fertility in rats. *Pregnancy*: See Warnings. *Nonteratogenic Effects*: The child born of a mother on benzodiazepines may be at some risk for withdrawal symptoms, neonatal flaccidity and respiratory problems. *Labor and Delivery*: No established use. *Nursing Mothers*: Benzodiazepines are excreted in human milk. Women on XANAX should not nurse. *Pediatric Use*: Safety and effectiveness in children below the age of 18 have not been established.

**ADVERSE REACTIONS**

Side effects are generally observed at the beginning of therapy and usually disappear with continued medication. In the usual patient, the most frequent side effects are likely to be an extension of the pharmacologic activity of XANAX, e.g., drowsiness or lightheadedness.

*Central nervous system*: Drowsiness, lightheadedness, depression, headache, confusion, insomnia, nervousness, syncope, dizziness, akathisia, and tiredness/sleepiness. *Gastrointestinal*: Dry mouth, constipation, diarrhea, nausea/vomiting, and increased salivation. *Cardiovascular*: Tachycardia/palpitations, and hypotension. *Sensory*: Blurred vision. *Musculoskeletal*: Rigidity and tremor. *Cutaneous*: Dermatitis/allergy. *Other side effects*: Nasal congestion, weight gain, and weight loss.

Withdrawal seizures with rapid decrease or abrupt discontinuation. (See Warnings.)

The following adverse events have been reported with benzodiazepines: dystonia, irritability, concentration difficulties, anorexia, transient amnesia or memory impairment, loss of coordination, fatigue, seizures, sedation, slurred speech, jaundice, musculoskeletal weakness, pruritus, diplopia, dysarthria, changes in libido, menstrual irregularities, incontinence, and urinary retention.

Paradoxical reactions such as stimulation, agitation, rage, increased muscle spasticity, sleep disturbances, and hallucinations may occur. Should these occur, discontinue the drug.

During prolonged treatment, periodic blood counts, urinalysis, and blood chemistry analysis are advisable. Minor EEG changes, of unknown significance, have been observed.

Liver enzyme elevations, gynecomastia and galactorrhea have been reported but no causal relationship was established.

**DRUG ABUSE AND DEPENDENCE**

*Physical and Psychological Dependence*: Withdrawal symptoms including seizures have occurred following abrupt discontinuance or rapid dose reduction of benzodiazepines. (See Warnings.) Dosage should be gradually tapered under close supervision. Patients with a history of seizures or epilepsy should not be abruptly withdrawn from XANAX. Addiction-prone individuals should be under careful surveillance. *Controlled Substance Class*: XANAX is a controlled substance and has been assigned to schedule IV.

**OVERDOSAGE**

Manifestations include somnolence, confusion, impaired coordination, diminished reflexes and coma. No delayed reactions have been reported.

**DOSAGE AND ADMINISTRATION**

Dosage should be individualized.

The usual starting dose is 0.25 to 0.5 mg, t.i.d. Maximum total daily dose is 4 mg. In the elderly or debilitated, the usual starting dose is 0.25 mg, two or three times daily. Reduce dosage gradually when terminating therapy, by no more than 0.5 mg every three days.

**HOW SUPPLIED**

XANAX Tablets are available as 0.25 mg, 0.5 mg, and 1 mg tablets.

**CAUTION:** FEDERAL LAW PROHIBITS DISPENSING WITHOUT PRESCRIPTION.

B-8-S
J-2252
November, 1989

Upjohn THE UPJOHN COMPANY
Kalamazoo, Michigan 49001, USA

Printed in USA

# THE MANFRED S. GUTTMACHER AWARD

The American Psychiatric Association and the American Academy of Psychiatry and the Law invite applications for the 1991 Manfred S. Guttmacher Award.

This award is given for an outstanding contribution to the literature of forensic psychiatry in the form of a book, monograph, paper, or any other work presented at a professional meeting or published between May 1, 1989, and April 30, 1990. The award will be formally presented in May 1991 at the American Academy of Psychiatry and the Law meeting held in conjunction with the American Psychiatric Association Annual Meeting in New Orleans. The award includes an honorarium of $500 and a plaque. The travel expenses of a nonmember winner will be reimbursed up to $500. The recipient is expected to give an award lecture. The award will be cited in the Convocation of Fellows program of the 1991 APA Annual Meting.

Anyone wishing to apply should submit six copies of work, along with six copies of an abstract to William H. Reid, M.D., M.P.H., Chairman, Guttmacher Award Board, American Psychiatric Association, 1400 K Street, N.W., Suite 327, Washington, DC 20005.

***Entries must be received by May 15, 1990. Entries will be acknowledged but not returned.***

Psychiatry Today

ADVERTISEMENT

# BREAKTHROUGH

## FOR THOUSANDS OF PROBLEM SCHIZOPHRENIC PATIENTS AND THEIR PSYCHIATRISTS

## Sandoz Introduces CLOZARIL® (clozapine) — A Breakthrough Antipsychotic Agent

### For Patients Who Fail to Respond Adequately to Treatment With Appropriate Courses of Standard Antipsychotic Drugs

Sandoz Pharmaceuticals Corporation has nnounced the introduction of CLOZARIL clozapine), a new, atypical antipsychotic gent that has demonstrated efficacy against ymptoms of schizophrenia in severely ill "problem") patients who fail to respond dequately to treatment with appropriate ourses of standard antipsychotic drugs. The rug, whose pharmacologic profile suggests unique mode of action, is being hailed as he first breakthrough in antipsychotic ther- py in more than two decades. In a clinical rial, as reported by John Kane, MD, and thers in an original article published in *rchives of General Psychiatry*, September 988, CLOZARIL (clozapine) proved significantly more effective than chlorpromazine in controlling both the positive and negative symptoms of chronic schizophrenia.

"CLOZARIL poses a very exciting opportunity," said John Kane, MD, chairman of the department of psychiatry, Hillside Hospital–Long Island Jewish Medical Center, and a key CLOZARIL investigator. "Our multicenter study suggests that the drug may be an important therapeutic advance in the treatment of schizophrenia." Other investigators have reported similar successes with CLOZARIL (clozapine) in many severely ill ("problem") schizophrenics who failed to respond adequately to treatment with

*(Continued on page 3)*

## Haloperidol Failures Respond

Chronic schizophrenics who had failed respond to a six-week course of haloper- lol showed significant improvement with LOZARIL® therapy in the landmark mul- center clinical trial. Symptoms began to nprove within two weeks after CLOZARIL erapy was begun. Improvement continued roughout the course of the study.

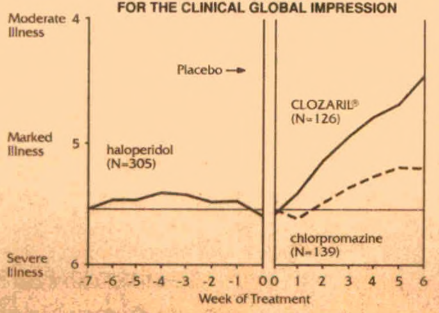
Study subjects were selected on the basis a history of failure to respond to standard ntipsychotic therapy. Prospective criteria cluded treatment failure on at least 60 mg/ y of haloperidol. After six weeks, only 6% of the patients treated with haloperidol d responded positively. Others failed to spond or were not able to tolerate the drug.

When treated with CLOZARIL (cloza- ne), haloperidol nonresponders demon- rated significant improvement in a broad nge of symptoms on the Brief Psychiatric ating Scale (BPRS), including the positive mptom cluster of thought disturbances: llucinations, unusual thought content, andiosity and conceptual disorganization.

Many CLOZARIL-treated patients were rated significantly improved in the negative symptom cluster of anergia. The initial response to CLOZARIL therapy was dramatic and achieved statistical significance after only two weeks of treatment.

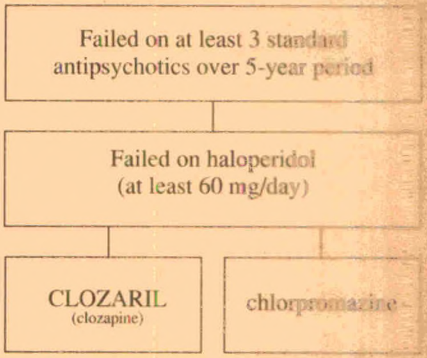
Researchers concluded that some 30% of CLOZARIL-treated patients showed significant improvement in overall clinical condition in only six weeks. Similar results were seen in only 4% of chlorpromazine-treated patients. ■

MEAN SCORES FOR THE CLINICAL GLOBAL IMPRESSION



## Rigorous Study Shows Superior Efficacy

In a landmark U.S. multicenter trial, CLOZARIL® (clozapine) proved to have greater efficacy than chlorpromazine in problem schizophrenics who had previously failed on haloperidol.


Failed on at least 3 standard antipsychotics over 5-year period
Failed on haloperidol (at least 60 mg/day)
CLOZARIL (clozapine)
chlorpromazine

According to Dr. Kane, the unusual protocol of the CLOZARIL trial had few precedents. "Many people thought this was an inordinately conservative test that really stacked the deck against clozapine," the investigator said.

Patients were first selected on the basis of a history of failure to respond to at least three drugs from two antipsychotic classes over the previous five years. They were then treated with at least 60 mg/day of haloperidol and 6 mg/day of benztropine for up to six weeks. Patients who failed to respond were randomized into two groups — one treated with CLOZARIL (clozapine) and one with chlorpromazine plus benztropine. Prophylactic benztropine was employed in the chlorpromazine group to mask extrapyramidal side effects and help maintain double-blind conditions. In this population of haloperidol failures, CLOZARIL (clozapine) demonstrated significant superiority over chlorpromazine in the treatment of positive and negative schizophrenic symptoms. ■

# Positive and Negative Symptoms Respond to CLOZARIL® (clozapine)

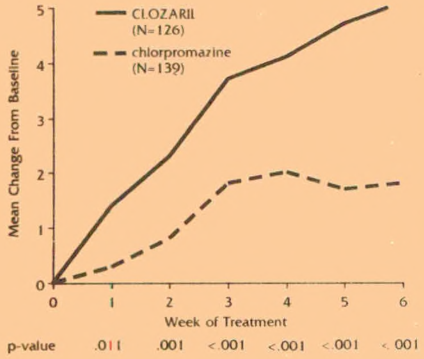
Dramatic evidence from a double-blind multicenter U.S. trial, published in the *Archives of General Psychiatry*, September 1988, indicates that CLOZARIL (clozapine) is effective against both "positive" and "negative" symptoms of schizophrenia in severely ill ("problem") patients who failed to respond adequately to treatment with appropriate courses of standard antipsychotic drugs. Within the first two weeks of CLOZARIL treatment, patients improved in several key areas of positive or florid symptomatology as measured on the Brief Psychiatric Rating Scale (BPRS): conceptual disorganization, suspiciousness, hallucinatory behavior, unusual thought content. CLOZARIL patients showed substantial improvement earlier and to a far greater degree than control patients treated with chlorpromazine.

Although the positive symptoms of schizophrenia have traditionally received the most clinical attention, there is growing
evidence that it is the
symptoms of schizophr
of the chronic disabil
tients. According to
Meltzer, MD, professo
Western Reserve Unive
cine, "The really re
CLOZARIL has been i
the deficit state, the ap
tion and loss of social

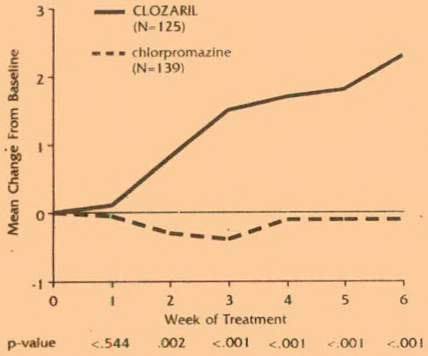
Patients treated
(clozapine) for six wee
nificant improvement
key negative symptom
emotional withdrawal
blunted affect and diso
negative symptoms in
group treated with chlo
unchanged. ■

**REPRESENTATIVE POSITIVE SYMPTOMS**
Conceptual
disorganization
Suspiciousness
Hallucinations
Delusions
(unusual thought
content)

**BRIEF PSYCHIATRIC RATING SCALE CLUSTER OF FOUR POSITIVE SYMPTOMS**
(conceptual disorganization, suspiciousness, hallucinatory behavior, unusual thought content)



**BRIEF PSYCHIATRIC RATING SCALE ANERGIA FACTOR**



# Unique Pa
# Controls B

The risk of CLOZA
ulocytosis can now be
investigators say, with t
Clozaril Patient Man
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Although CLOZA
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standard antipsychotic
of potentially fatal agr
estimates indicate a
CLOZARIL (clozapin

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be recognized early.
sharply when clinician
need to monitor whit
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as a major drop in WB
In U.S. clinical trials
use programs through
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INTRODUCING

A BEACON OF
HOPE

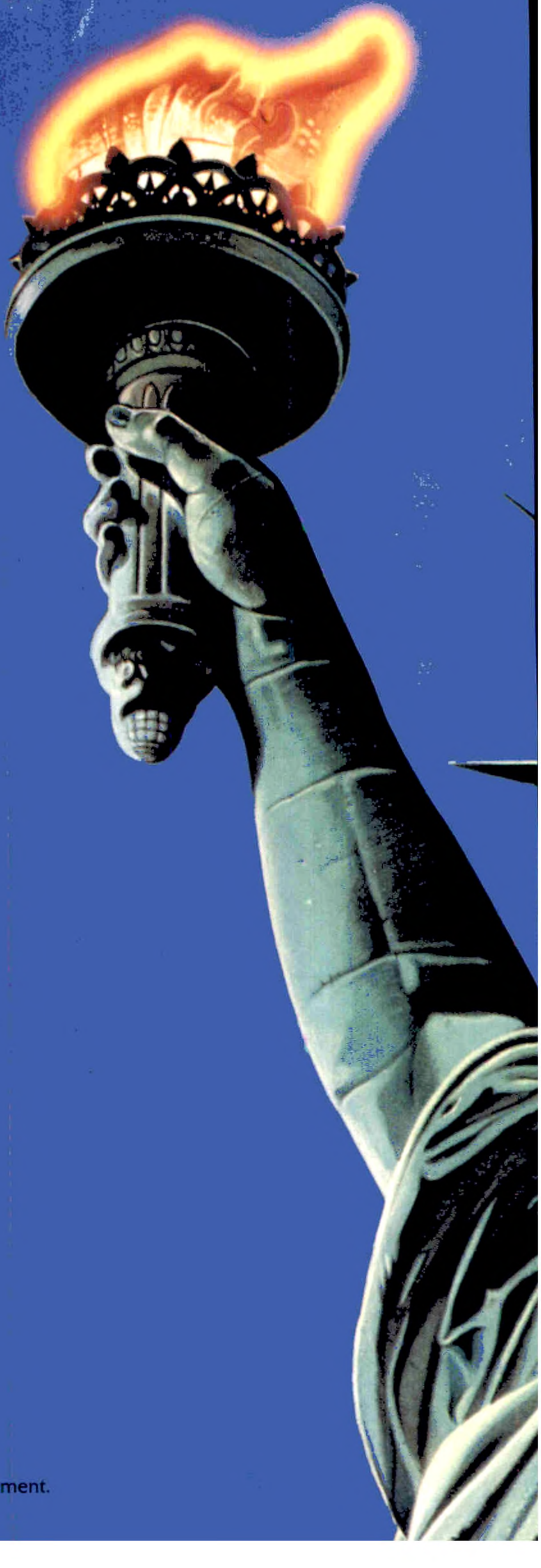
FOR THOUSANDS
OF PROBLEM SCHIZOPHRENIC
PATIENTS
AND THEIR PSYCHIATRISTS

NEW

CLOZARIL®

(clozapine)

SUPERIOR
ANTIPSYCHOTIC
EFFICACY
THAT
GIVES HOPE
FOR
A
NEW
BEGINNING



Please see brief summary of prescribing information following this advertisement.
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## HOPE BEGINS WITH SUPERIOR SYMPTOMATIC CONTROL[*]

In a six-week controlled study in severely ill ("problem") schizophrenic patients who failed to respond adequately to treatment with appropriate courses of standard antipsychotic drugs:

- CLOZARIL® (clozapine) succeeded after standard antipsychotics, including haloperidol, failed
- Thirty percent of CLOZARIL patients experienced dramatic global improvement in only six weeks (as determined by the study's rigorous efficacy criteria) vs only 4% of patients receiving chlorpromazine
- Efficacy in both positive and negative symptomatology

## HOPE CONTINUES WITH A VIRTUAL ABSENCE OF CERTAIN ACUTE EXTRAPYRAMIDAL SYMPTOMS

- CLOZARIL® (clozapine) is indicated for patients intolerant of standard antipsychotics
- No confirmed cases of tardive dyskinesia in over 15 years' worldwide experience
- Side effects that have been reported include: agranulocytosis (1–2%), transient sedation (39%), hypersalivation (31%), tachycardia (25%), constipation (14%), hypotension (9%), hypertension (4%) and weight gain (4%)[†]
- CLOZARIL use is associated with a substantial risk of seizure, an apparently dose-dependent reaction affecting 1–2% of patients at low doses (below 300 mg/day), 3–4% at moderate doses, and 5% at high doses (600–900 mg/day)[‡]

## HOPE IS MAINTAINED THROUGH A MANDATORY WBC MONITORING SYSTEM WHICH HELPS MANAGE THE RISK OF AGRANULOCYTOSIS

- Agranulocytosis, a potentially fatal disorder, occurs in 1–2% of patients
- The Clozaril Patient Management System℠ (CPMS℠) was created as an efficient means to detect developing agranulocytosis
- This structured weekly monitoring and drug delivery system helps to protect the patient and to support the physician

**CLOZARIL®**

(clozapine)

25 mg and 100 mg tablets

**CLOZARIL therapy is available only through the Clozaril Patient Management System. Call 1-800-237-CPMS (2767) or mail in a completed CPMS patient enrollment form to prescribe CLOZARIL (clozapine). Contact your Sandoz Mental Health Sales Representative for general information on CLOZARIL (clozapine) and the Clozaril Patient Management System.**

---

[*] In a double-blind study of CLOZARIL (clozapine) versus chlorpromazine encompassing 268 patients, all of whom had first failed on at least three standard antipsychotics over a five-year period and then on a trial of high-dose haloperidol.

INTRODUCING

# CLOZARIL®
(clozapine)

## A BEACON OF HOPE FOR PROBLEM SCHIZOPHRENIC PATIENTS

**To prescribe**
**CLOZARIL**
**(clozapine)**
**call 1-800-237-CPMS (2767)**
**or mail in a completed CPMS patient enrollment form.**

†Tachycardia, hypotension and hypertension are the principal cardiovascular effects associated with CLOZARIL (clozapine).

‡Because of the substantial risk of seizure associated with CLOZARIL use, a dosage ceiling of 600 mg/day is recommended, although some patients may require up to 900 mg/day for a therapeutic effect.

## HOPE FOR A NEW BEGINNING

**CLOZARIL®**
(clozapine)
25 mg and 100 mg tablets

**SANDOZ**PHARMACEUTICALS
Corporation, E. Hanover, NJ 07936 (201) 503-7500

Please see brief summary of prescribing information following this advertisement. Printed in U.S.A. 1/90 CLO-0989-02

# BREAKTHROUGH

*(Continued from page 1)*

propriate courses of standard antipsychotic
igs. Herbert Meltzer, MD, Douglas Dan-
d Bond Professor of Psychiatry at Case
stern Reserve University School of Medi-
e, demonstrated the effect of 6–9 months'
atment with CLOZARIL® (clozapine) on
ial function and interpersonal relation-
ps in 21 problem schizophrenic patients.
cording to Dr. Meltzer, "The extent of
provement in the QLS [Quality of Life
ale] scores after 6 months' clozapine treat-
nt was impressive. Total QLS scores
rly tripled during this period. Total QLS
res at least doubled in 76% of the patients.
e improvement was most marked in the
a of ability to work or return to school, but
s also strong in intrapsychic foundations
l interpersonal relations."

The new drug has created considerable
citement among families of chronic
izophrenic patients. As one parent said,
or us, CLOZARIL (clozapine) means new
pe, and that's been a scarce commodity
ong schizophrenic patients and their
nilies."

Because of its unique pharmacologic pro-
, CLOZARIL (clozapine) is thought to
ve a somewhat different mode of action
n standard antipsychotics. The new drug
haracterized by a virtual absence of certain acute extrapyramidal symptoms (e.g., dystonia). Also, unlike standard antipsychotics, it causes little or no elevation in serum prolactin levels and has not been linked to any confirmed cases of tardive dyskinesia.

However, it does carry an increased risk of seizure and agranulocytosis, necessitating weekly blood monitoring for all patients. The incidence of agranulocytosis, a potentially fatal disorder, associated with CLOZARIL (clozapine) is 1–2%. In Europe — principally before 1977 — prior to recognition and management of the risk, a number of fatalities occurred. With mandatory weekly white blood cell (WBC) monitoring, all cases in the United States through mid-1989 (15 in over 1,700 patients) have reversed, and no fatalities have occurred. ■

## emple University
## ccredits
## LOZARIL®
## ducational Program

Temple University has accredited the
OZARIL Educational Program devel-
ed by Sandoz Pharmaceuticals Corpora-
n to ensure safe and efficacious use of this
v atypical antipsychotic agent. A series of
conference workshops will be held at
r 600 sites across the country. Physicians
o participate will receive 4 hours of CME
dit for attending the conference and com-
ting the self-study materials.

These regional workshops will feature
eotaped presentations and live interactive
cussions via two-way telephone hookups.
is will allow CLOZARIL investigators
l other experts to answer audience ques-
ns on the spot. Psychiatrists and allied
lthcare professionals attending the work-
ps will receive information about the
efits and risks of CLOZARIL therapy
l the appropriate selection and manage-
nt of patients.

Comprehensive take-home materials will
lude prescribing and product information,
sychiatrist's guide to CLOZARIL-associ-
d agranulocytosis and a detailed descrip-
n of the Clozaril Patient Management
stem$^{SM}$ (CPMS$^{SM}$). ■

## Side Effects Profile Further Distinguishes CLOZARIL® (clozapine)

Because of its unique pharmacologic profile, CLOZARIL (clozapine) appears to have a more specific mechanism of action than standard antipsychotics. This may be the reason for the virtual absence of certain acute extrapyramidal side effects — and no confirmed cases of tardive dyskinesia. Researchers theorize that this is because the drug has been shown in animal studies to be more selective for dopamine receptors in the limbic area of the brain, rather than the striatal receptors affected by most standard antipsychotics. In addition, in both preclinical and clinical studies, CLOZARIL (clozapine) causes little or no elevation of serum prolactin levels, and thus tends not to produce prolactin-related side effects as do other antipsychotic drugs.

CLOZARIL (clozapine) is, however, associated with a higher incidence of agranulocytosis than standard antipsychotics — 1–2% as compared with 0.1% for standard agents. Careful monitoring through the Clozaril Patient Management System$^{SM}$ (CPMS$^{SM}$) will help promote early detection and timely drug discontinuation. Other side effects that have been reported include transient sedation (39%), hypersalivation (31%), tachycardia (25%), constipation (14%), hypotension (9%), seizures (5%), hypertension (4%) and weight gain (4%).

CLOZARIL use is associated with a substantial risk of seizure, an apparently dose-dependent reaction affecting 1–2% of patients at low doses (below 300 mg/day), 3–4% at moderate doses, and 5% at high doses (600–900 mg/day). In the multicenter

*(Continued on page 4)*

## CLOZARIL® Researcher Recounts CLOZARIL History

"I've seen CLOZARIL (clozapine) through its ups and downs," said Gilbert Honigfeld, PhD, associate director of Sandoz Research Institute, who has piloted the drug's development since joining Sandoz in 1973. Honigfeld recounted how the drug was first discovered in 1960 by Swiss scientists at the Wander Division of Sandoz and was being used in Europe in the 1970s when reports of agranulocytosis appeared.

These reports led to cessation of active U.S. CLOZARIL research for a number of years. "But clinicians would not let go of it," Honigfeld recalled. Patients were given the drug on a compassionate need basis, and evidence continued to mount that not only did CLOZARIL (clozapine) have superior efficacy, but that the risk of agranulocytosis could be managed with careful monitoring. Sandoz resumed clinical R&D in the '80s, and submitted results of its rigorous study in severely ill schizophrenic patients to government health officials in August 1987. ■

## Reimbursement

Efforts are being made to ensure that the majority of patients selected for CLOZARIL® therapy will be eligible to have their Clozaril Patient Management System$^{SM}$ (CPMS$^{SM}$) costs reimbursed by third-party payers, such as state Medicaid programs and the Veterans Administration. Additionally, duration of hospitalization is expected to decrease for patients on CLOZARIL therapy. In one retrospective study, the time spent outside institutions increased from 44% before CLOZARIL treatment to 63% in the second year of treatment with CLOZARIL (clozapine). That results in significant savings in cost of care as former inpatients become outpatients. Around the country, enthusiasm is being expressed for the new medication, which is expected to reduce substantially the chronic care costs of schizophrenia in a limited patient population. ■

# Patient Management System a Success

Early detection is the key to safe management of CLOZARIL®-induced agranulocytosis. Clinicians are expressing approval of the new Clozaril Patient Management System℠ (CPMS℠), a comprehensive system of WBC testing, pharmacy, clinical laboratory and drug distribution services, all linked to compliance with required safety monitoring. The program has been tested in pilot studies across the U.S. and has achieved over 99% blood monitoring compliance on the part of the patients — without interfering with the physician's medical control.

The system is designed to detect falling WBC counts that may be indicative of impending agranulocytosis. In the event of abnormal test results, the physician will be notified immediately. If the abnormal test shows only a downward trend from a normal WBC count to a count that has not yet reached leukopenia, additional blood work, such as a complete blood count and a differential count, should be performed. If the WBC count stabilizes, the patient returns to the normal cycle of weekly monitoring.

*Patients who are discontinued from CLOZARIL (clozapine) because of severe leukopenia or agranulocytosis cannot resume therapy.* A single national database is maintained by CPMS in an effort to ensure that any patient who develops severe leukopenia or agranulocytosis is not rechallenged with CLOZARIL (clozapine).

Caremark Homecare, Inc., a national home healthcare agency, has been chosen to implement the system. CPMS Case Administrators arrange for patients' blood to be drawn weekly, and the samples sent for analysis to Roche Biomedical Laboratories, a national clinical laboratory. A Clozapak™ seven-day supply of CLOZARIL (clozapine) is released upon collection of blood samples. CPMS operates on the principle of "No blood, no drug" to ensure that CLOZARIL (clozapine) is administered in the safest possible manner. The drug will be obtainable only through the Clozaril Patient Management System.

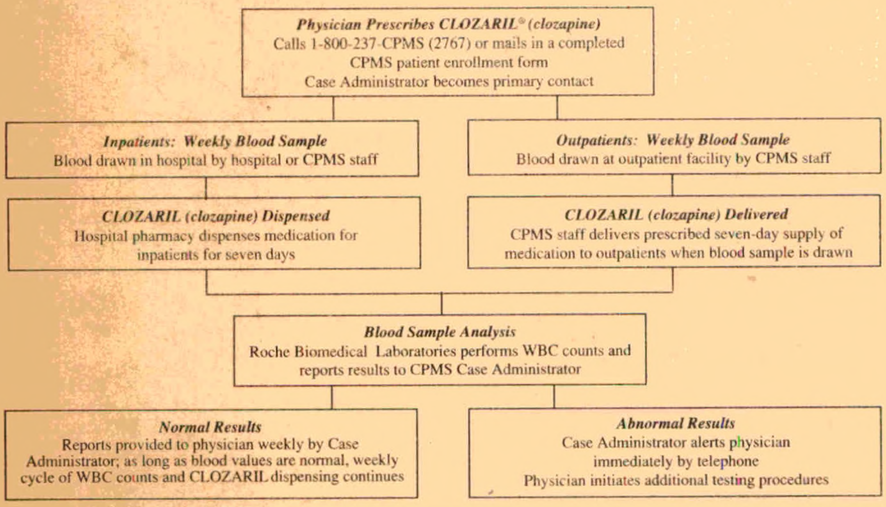
A CPMS Case Administrator coordinates WBC testing, reporting and drug delivery. For inpatients, weekly monitoring is performed in the hospital. Case Administrators arrange for weekly monitoring of outpatients. If a WBC test is missed, the Case Administrator will reschedule collection and pickup to transport the blood specimen to the laboratory.

When the patient's blood sample is collected, a week's supply of CLOZARIL (clozapine) is dispensed (see chart). Each week, results of the WBC count are sent to the prescribing psychiatrist. The Case Administrator will alert the psychiatrist immediately by telephone if the white blood cell count drops significantly.

In addition to its safety benefits, CPMS can also enhance clinical care, according to Richard Wagner, MD. Dr. Wagner is director of the Rhode Island Psychiatric Research and Training Center, one of 16 sites selected for the U.S. multicenter CLOZARIL comparative study. He said that the weekly patient follow-up provided by CPMS often improves compliance with the drug regimen and decreases recidivism. Some patients chronically hospitalized will respond so dramatically they can be discharged.

Clinicians who would like more information about CPMS may contact their Sandoz Mental Health Sales Representative. ■

## How the Clozaril Patient Management System℠ (CPMS℠) Works


Physician Prescribes CLOZARIL® (clozapine)
Calls 1-800-237-CPMS (2767) or mails in a completed CPMS patient enrollment form
Case Administrator becomes primary contact
Inpatients: Weekly Blood Sample
Blood drawn in hospital by hospital or CPMS staff
Outpatients: Weekly Blood Sample
Blood drawn at outpatient facility by CPMS staff
CLOZARIL (clozapine) Dispensed
Hospital pharmacy dispenses medication for inpatients for seven days
CLOZARIL (clozapine) Delivered
CPMS staff delivers prescribed seven-day supply of medication to outpatients when blood sample is drawn
Blood Sample Analysis
Roche Biomedical Laboratories performs WBC counts and reports results to CPMS Case Administrator
Normal Results
Reports provided to physician weekly by Case Administrator; as long as blood values are normal, weekly cycle of WBC counts and CLOZARIL dispensing continues
Abnormal Results
Case Administrator alerts physician immediately by telephone
Physician initiates additional testing procedures

# Side Effects Profile

*(Continued from page 3)*

study, the mean and median doses were both approximately 600 mg/day. Patients must be advised not to engage in any activity where sudden loss of consciousness could cause serious risk to themselves or others, e.g., the operation of complex machinery, driving an automobile, swimming, climbing, etc.

Particular attention should be paid to patients with underlying cardiovascular disease or arrhythmias. Sustained tachycardia is a frequent occurrence in patients (25%) taking CLOZARIL tablets, with patients having an average increase in pulse rate of 10-15 bpm. Hypotension (9%) and hypertension (4%) are other cardiovascular effects associated with CLOZARIL (clozapine). ■

# Management System Frees Psychiatrists From Routine Tasks

The Clozaril Patient Management System℠ (CPMS℠) relieves psychiatrists of the burden of hematological monitoring that must accompany CLOZARIL® therapy. The mandatory weekly white blood cell counts are conducted by Caremark Homecare, Inc., a national home healthcare agency, under the supervision of an agency Case Administrator, who arranges for the specimens to be transported and analyzed by Roche Biomedical Laboratories, a national clinical laboratory.

The physician need only call 1-800-237-CPMS (2767) to prescribe CLOZARIL (clozapine) or mail in a completed CPMS patient enrollment form. Thereafter, the Case Administrator will coordinate blood testing and drug dispensing, and report blood test results to the prescribing psychiatrist. At all times, the physician retains clinical control of the patient.

When the patient's WBC count is normal, the drug will be dispensed routinely, with the report mailed to the psychiatrist. Should a drop in WBC count occur, the psychiatrist will be contacted immediately by telephone. ■

# Investigators Report Virtual Absence of Certain Acute EPS

Unlike standard antipsychotics, a virtual absence of certain acute extrapyramidal side effects (EPS), such as acute dystonia, is associated with CLOZARIL® administration. The incidence of other EPS, such as akathisia and rigidity, is also much lower with CLOZARIL therapy than with other agents. In a double-blind comparison of CLOZARIL (clozapine) and chlorpromazine/benztropine, 11 of 76 chlorpromazine-treated patients discontinued therapy because of poorly tolerated EPS. In contrast, only one of 75 CLOZARIL patients stopped treatment because of EPS. There have been no confirmed cases of tardive dyskinesia in over 15 years' worldwide experience with clozapine. ■

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Please see brief summary of prescribing information on following page.

# CLOZARIL®

(clozapine)

TABLETS

**CAUTION: Federal law prohibits dispensing without a prescription.**

## CONTRAINDICATIONS

CLOZARIL is contraindicated in patients with myeloproliferative disorders, or a history of CLOZARIL-induced agranulocytosis or severe granulocytopenia. CLOZARIL should not be used simultaneously with other agents having a well-known potential to suppress bone marrow function. As with more typical antipsychotic drugs, CLOZARIL is contraindicated in severe central nervous system depression or comatose states from any cause.

## WARNINGS

### General

**BECAUSE OF THE SIGNIFICANT RISK OF AGRANULOCYTOSIS, A POTENTIALLY LIFE-THREATENING ADVERSE EVENT (SEE BELOW), CLOZARIL SHOULD BE RESERVED FOR USE IN THE TREATMENT OF SEVERELY ILL SCHIZOPHRENIC PATIENTS WHO FAIL TO SHOW AN ACCEPTABLE RESPONSE TO ADEQUATE COURSES OF STANDARD ANTIPSYCHOTIC DRUG TREATMENT, EITHER BECAUSE OF INSUFFICIENT EFFECTIVENESS OR THE INABILITY TO ACHIEVE AN EFFECTIVE DOSE DUE TO INTOLERABLE ADVERSE EFFECTS FROM THOSE DRUGS. CONSEQUENTLY, BEFORE INITIATING TREATMENT WITH CLOZARIL, IT IS STRONGLY RECOMMENDED THAT A PATIENT BE GIVEN AT LEAST TWO TRIALS, EACH WITH A DIFFERENT STANDARD ANTIPSYCHOTIC DRUG PRODUCT, AT AN ADEQUATE DOSE AND FOR AN ADEQUATE DURATION.**

**PATIENTS WHO ARE BEING TREATED WITH CLOZARIL MUST HAVE A BASELINE WHITE BLOOD CELL (WBC) AND DIFFERENTIAL COUNT BEFORE INITIATION OF TREATMENT, AND A WBC COUNT EVERY WEEK THROUGHOUT TREATMENT, AND FOR FOUR WEEKS AFTER THE DISCONTINUATION OF CLOZARIL.**

**CLOZARIL IS AVAILABLE ONLY THROUGH THE CLOZARIL PATIENT MANAGEMENT SYSTEM$^{SM}$ (CPMS$^{SM}$).**

### Agranulocytosis

**Agranulocytosis, defined as a granulocyte count (polys + bands) of less than 500 per $mm^3$, has been estimated to occur in association with CLOZARIL use at a cumulative incidence at one year of approximately 1.3%, based on the occurrence of 15 U.S. cases out of 1743 patients exposed to CLOZARIL during its clinical testing prior to domestic marketing. All of these cases occurred at a time when the need for close monitoring of WBC counts was already recognized. This reaction could prove fatal if not detected early and therapy interrupted. While no fatalities have been associated with the U.S. agranulocytosis cases, and all cases have recovered fully, the U.S. sample is too small to reliably estimate the case fatality rate. Of the 112 cases of agranulocytosis reported worldwide in association with CLOZARIL use as of December 31, 1986, 35% were fatal. However, few of these deaths occurred since 1977, at which time the knowledge of CLOZARIL-induced agranulocytosis became more widespread, and close monitoring of WBC counts more widely practiced. Nevertheless, it is unknown at present what the case fatality rate will be for CLOZARIL-induced agranulocytosis, despite strict adherence to the recommendation for weekly monitoring of WBC counts.**

**Treatment should not be initiated if the WBC count is less than 3500 per $mm^3$, or if the patient has a history of a myeloproliferative disorder, or previous CLOZARIL-induced agranulocytosis or granulocytopenia. Patients should be advised to report immediately the appearance of lethargy, weakness, fever, sore throat or any other signs of infection. If, after the initiation of treatment, the total WBC count has dropped below 3500 per $mm^3$ or it has dropped by a substantial amount from baseline, even if the count is above 3500 per $mm^3$, or if immature forms are present, a repeat WBC count and a differential count should be done. If subsequent WBC counts and the differential count reveal a total WBC count between 3000 and 3500 per $mm^3$ and a granulocyte count above 1500 per $mm^3$, twice weekly WBC counts and differential counts should be performed.**

**If the total WBC count falls below 3000 per $mm^3$ or the granulocyte count below 1500 per $mm^3$, CLOZARIL therapy should be interrupted and patients should be carefully monitored for flu-like symptoms or other symptoms suggestive of infection. CLOZARIL therapy may be resumed if no symptoms of infection develop, and if the total WBC count returns to levels above 3000 per $mm^3$ and the granulocyte count returns to levels above 1500 per $mm^3$. However, in this event, twice-weekly WBC counts and differential counts should continue until total WBC counts return to levels above 3500 per $mm^3$.**

**If the total WBC count falls below 2000 per $mm^3$ or the granulocyte count falls below 1000 per $mm^3$, bone marrow aspiration should be considered to ascertain granulopoietic status. Protective isolation with close observation may be indicated if granulopoiesis is determined to be deficient. Should evidence of infection develop, the patient should have appropriate cultures performed and an appropriate antibiotic regimen instituted.**

**Patients whose total WBC counts fall below 2000 per $mm^3$, or granulocyte counts below 1000 per $mm^3$ during CLOZARIL therapy should *not* be re-challenged with CLOZARIL. Patients discontinued from CLOZARIL therapy due to significant WBC suppression have been found to develop agranulocytosis upon re-challenge, often with a shorter latency on re-exposure. To reduce the chances of re-challenge occurring in patients who have experienced significant bone marrow suppression during CLOZARIL therapy, a single, national master file will be maintained confidentially within the CPMS (Clozaril Patient Management System).**

**Except for evidence of significant bone marrow suppression during initial CLOZARIL therapy, there are no established risk factors, based on worldwide experience, for the development of agranulocytosis in association with CLOZARIL use. However, a disproportionate number of the U.S. cases of agranulocytosis occurred in patients of Jewish background compared to the overall proportion of such patients exposed during the domestic development of CLOZARIL. Most of the U.S. cases occurred within 4-10 weeks of exposure, but neither dose nor duration is a reliable predictor of this problem. No patient characteristics have been clearly linked to the development of agranulocytosis in association with CLOZARIL use, but agranulocytosis associated with other antipsychotic drugs has been reported to occur with a greater frequency in women, the elderly and in patients who are cachectic or have serious underlying medical illness; such patients may also be at particular risk with CLOZARIL.**

**To reduce the risk of agranulocytosis developing undetected, CLOZARIL will be dispensed only within the Clozaril Patient Management System.**

### Seizures

**Seizure has been estimated to occur in association with CLOZARIL use at a cumulative incidence at one year of approximately 5%, based on the occurrence of one or more seizures in 61 of 1743 patients exposed to CLOZARIL during its clinical testing prior to domestic marketing (i.e., a crude rate of 3.5%). Dose appears to be an important predictor of seizure, with a greater likelihood of seizure at the higher CLOZARIL doses used.**

**Caution should be used in administering CLOZARIL to patients having a history of seizures or other predisposing factors. Because of the substantial risk of seizure associated with CLOZARIL use, patients should be advised not to engage in any activity where sudden loss of consciousness could cause serious risk to themselves or others, e.g., the operation of complex machinery, driving an automobile, swimming, climbing, etc.**

### Adverse Cardiovascular Effects

Orthostatic hypotension can occur with CLOZARIL treatment, especially during initial titration in association with rapid dose escalation, and may represent a continuing risk in some patients. Tachycardia, which may be sustained, has also been observed in approximately 25% of patients taking CLOZARIL, with patients having an average increase in pulse rate of 10-15 bpm. The sustained tachycardia is not simply a reflex response to hypotension, and is present in all positions monitored. Either tachycardia or hypotension may pose a serious risk for an individual with compromised cardiovascular function. A minority of CLOZARIL-treated patients experience ECG repolarization changes similar to those seen with other antipsychotic drugs, including S-T segment depression and flattening or inversion of T waves, which all normalize after discontinuation of CLOZARIL. The clinical significance of these changes is unclear. However, in clinical trials with CLOZARIL, several patients experienced significant cardiac events, including ischemic changes, myocardial infarction, nonfatal arrhythmias and sudden unexplained death. Causality assessment was difficult in many of these cases because of serious preexisting cardiac disease and plausible alternative causes. Rare instances of sudden, unexplained death have been reported in psychiatric patients, with or without associated antipsychotic drug treatment, and the relationship of these events to antipsychotic drug use is unknown. CLOZARIL should be used with caution in patients with known cardiovascular disease, and the recommendation for gradual titration of dose should be carefully observed.

### Neuroleptic Malignant Syndrome

A potentially fatal symptom complex sometimes referred to as Neuroleptic Malignant Syndrome (NMS) has been reported in association with antipsychotic drugs. Clinical manifestations of NMS are hyperpyrexia, muscle rigidity, altered mental status and evidence of autonomic instability (irregular pulse or blood pressure, tachycardia, diaphoresis, and cardiac dysrhythmias). No cases of NMS have been attributed to CLOZARIL alone. However, there have been several reported cases of NMS in patients treated concomitantly with lithium or other CNS-active agents.

### Tardive Dyskinesia

A syndrome consisting of potentially irreversible, involuntary, dyskinetic movements may develop in patients treated with antipsychotic drugs. Although the prevalence of the syndrome appears to be highest among the elderly, especially elderly women, it is impossible to rely upon prevalence estimates to predict, at the inception of treatment, which patients are likely to develop the syndrome.

There are several reasons for predicting that CLOZARIL may be different from other antipsychotic drugs in its potential for inducing tardive dyskinesia, including the preclinical finding that it has a relatively weak dopamine blocking effect and the clinical finding of a virtual absence of certain acute extrapyramidal symptoms, e.g., dystonia. In addition, there have been no confirmed cases of tardive dyskinesia developing in association with CLOZARIL use. Nevertheless, it cannot yet be concluded, without more extended experience, that CLOZARIL is incapable of inducing this syndrome.

## PRECAUTIONS

Because of the significant risk of agranulocytosis and seizure, both of which present a continuing risk over time, the extended treatment of patients failing to show an acceptable level of clinical response should ordinarily be avoided. In addition, the need for continuing treatment in patients exhibiting beneficial clinical responses should be periodically re-evaluated. During CLOZARIL therapy, patients may experience transient temperature elevations above 100.4°F (38°C), with the peak incidence within the first three weeks of treatment. While this fever is generally benign and self-limiting, it may necessitate discontinuing patients from treatment. On occasion, there may be an associated increase or decrease in WBC count. Patients with fever should be carefully evaluated to rule out the possibility of an underlying infectious process or the development of agranulocytosis. In the presence of high fever, the possibility of neuroleptic malignant syndrome (NMS) must be considered. CLOZARIL has very potent anticholinergic effects, and great care should be exercised in using this drug in the presence of prostatic enlargement or narrow angle glaucoma. Because of initial sedation, CLOZARIL may impair mental and/or physical abilities, especially during the first few days of therapy. The recommendations for gradual dose escalation should be carefully adhered to, and patients cautioned about activities requiring alertness. Clinical experience with CLOZARIL in patients with concomitant systemic diseases is limited. Nevertheless, caution is advisable in using CLOZARIL in patients with hepatic, renal or cardiac disease.

### Information for Patients

Patients who are to receive CLOZARIL should be warned about the significant risk of developing agranulocytosis. They should be informed that weekly blood tests are required to monitor for the occurrence of agranulocytosis, and that CLOZARIL tablets will be made available only through a special program designed to ensure the required blood monitoring. Patients should be advised to report immediately the appearance of lethargy, weakness, fever, sore throat, malaise, mucous membrane ulceration or other possible signs of infection. Particular attention should be paid to any flu-like complaints or other symptoms that might suggest infection. Patients should be informed of the significant risk of seizure during CLOZARIL treatment, and they should be advised to avoid driving and any other potentially hazardous activity while taking CLOZARIL. Patients should be advised of the risk of orthostatic hypotension, especially during the period of initial dose titration. Patients should notify their physician if they are taking, or plan to take, any prescription or over-the-counter drugs or alcohol. Patients should notify their physician if they become pregnant or intend to become pregnant during therapy. Patients should not breast feed an infant if they are taking CLOZARIL.

**CLOZARIL®**

(clozapine)

TABLETS

**Drug Interactions**

The risks of using CLOZARIL in combination with other drugs have not been systematically evaluated. The mechanism of CLOZARIL-induced agranulocytosis is unknown; nonetheless, the possibility that causative factors may interact synergistically to increase the risk and/or severity of bone marrow suppression warrants consideration. Therefore, CLOZARIL should not be used with other agents having a well-known potential to suppress bone marrow function. Given the primary CNS effects of CLOZARIL, caution is advised in using it concomitantly with other CNS-active drugs. Because CLOZARIL is highly bound to serum protein, the administration of CLOZARIL to a patient taking another drug which is highly bound to protein (e.g., warfarin, digoxin) may cause an increase in plasma concentrations of these drugs, potentially resulting in adverse effects. Conversely, adverse effects may result from displacement of protein-bound CLOZARIL by other highly bound drugs.

**CLOZARIL may also potentiate the hypotensive effects of antihypertensive drugs and the anticholinergic effects of atropine-type drugs. The administration of epinephrine should be avoided in the treatment of drug-induced hypotension because of a possible reverse epinephrine effect.**

**Pregnancy Category B**

There are no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, and in view of the desirability of keeping the administration of all drugs to a minimum during pregnancy, this drug should be used only if clearly needed.

**ADVERSE REACTIONS**

Adverse events observed in association with the use of CLOZARIL in clinical trials at an incidence of 5% or greater were: central nervous system complaints, including drowsiness/sedation, dizziness/vertigo, headache and tremor; autonomic nervous system complaints, including salivation, sweating, dry mouth and visual disturbances; cardiovascular findings, including tachycardia, hypotension and syncope; and gastrointestinal complaints, including constipation and nausea; and fever. Complaints of drowsiness/sedation tend to subside with continued therapy or dose reduction. Salivation may be profuse, especially during sleep, but may be diminished with dose reduction.

**DOSAGE AND ADMINISTRATION**

**Initial Treatment**

It is recommended that treatment with CLOZARIL begin at 25 mg once or twice daily, and then be continued with daily dosage increments of 25 to 50 mg/day, if well-tolerated, to achieve a target dose of 300 to 450 mg/day by the end of two weeks. Subsequent dosage increments should be made no more than once- or twice-weekly, in increments not to exceed 100 mg. Cautious titration and a divided dosage schedule are necessary to minimize the risks of hypotension, seizure, and sedation.

**Therapeutic Dose Adjustment**

Daily dosing should continue on a divided basis as an effective and tolerable dose level is sought. While many patients may respond adequately at doses between 300-600 mg/day, it may be necessary to raise the dose to the 600-900 mg/day range to obtain an acceptable response. [Note: In the multicenter study providing the primary support for the superiority of CLOZARIL in treatment resistant patients, the mean and median CLOZARIL doses were both approximately 600 mg/day.]

Because of the possibility of increased adverse reactions at higher doses, particularly seizures, patients should ordinarily be given adequate time to respond to a given dose level before escalation to a higher dose is contemplated.

Dosing should not exceed 900 mg/day.

**Discontinuation of Treatment**

In the event of planned termination of CLOZARIL therapy, gradual reduction in dose is recommended over a 1 to 2 week period. However, should a patient's medical condition require abrupt discontinuation (e.g., leukopenia), the patient should be carefully observed for the recurrence of psychotic symptoms.

**CLOZARIL is available only through the Clozaril Patient Management System, a program that combines white blood cell testing, patient monitoring, pharmacy, and drug distribution services, all linked to compliance with required safety monitoring.**

**To prescribe CLOZARIL call 1-800-237-CPMS (2767) or mail in a completed CPMS Enrollment Form.**

**SANDOZ**PHARMACEUTICALS
Corporation, E. Hanover, NJ 07936 (201) 503-7500

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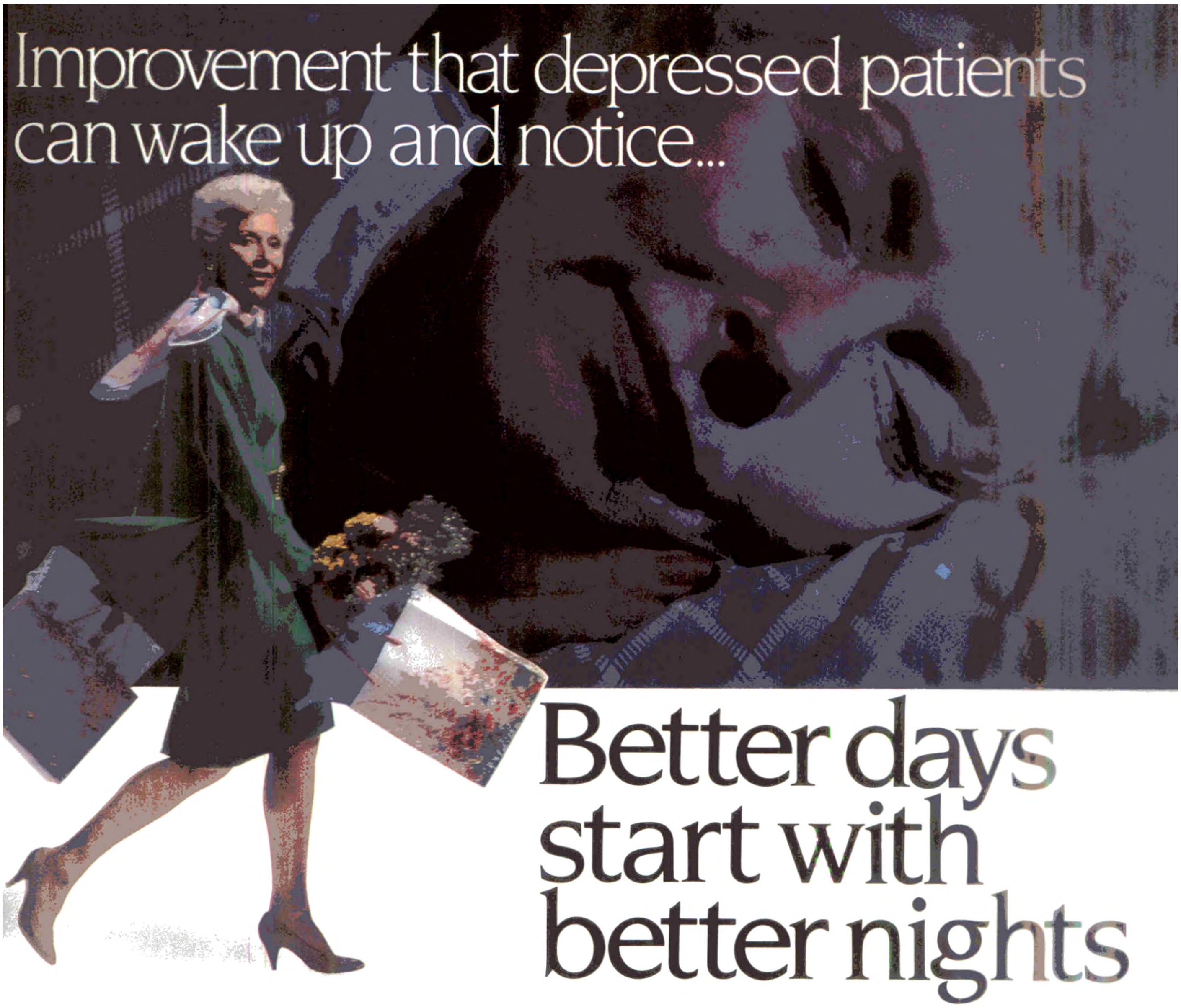
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# Better days start with better nights

- Up to 97% of depressed patients experience some kind of sleep disturbance, and often it may be the presenting sign.[1]
- Sleep disturbances respond particularly well to once-a-day Sinequan® (doxepin HCl)... as it works to relieve underlying depression and anxiety.[2,3]

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*Please see brief summary of SINEQUAN® (doxepin HCl) prescribing information on next page.*

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**References: 1.** Goldberg HL: Sleep disturbance as a manifestation of depression, in *Somatic Depression: Insights for Primary Care Physicians*. Proceedings of a symposium held in Miami, Dec 4, 1978. New York, Postgraduate Medicine Communications, pp 13-18. **2.** Karacan I, Blackburn AB, Thornby JI, et al: The effect of doxepin HCl (Sinequan) on sleep patterns and clinical symptomatology of neurotic depressed patients with sleep disturbance, in *Sinequan® (doxepin HCl): A Monograph of Recent Clinical Studies*. Princeton, NJ, Excerpta Medica, 1977, pp 4-22. **3.** Goldberg HL, Finnerty RJ: The use of doxepin in the treatment of symptoms of anxiety neurosis and accompanying depression: A collaborative controlled study. *Am J Psychiatry* 1972;129(July):74-77.

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# SINEQUAN® (doxepin HCl)

**BRIEF SUMMARY**
**SINEQUAN® (doxepin HCl) Capsules/Oral Concentrate**

**Contraindications.** SINEQUAN is contraindicated in individuals who have shown hypersensitivity to the drug. Possibility of cross sensitivity with other dibenzoxepines should be kept in mind.

SINEQUAN is contraindicated in patients with glaucoma or a tendency to urinary retention. These disorders should be ruled out, particularly in older patients.

**Warnings.** The once-a-day dosage regimen of SINEQUAN in patients with intercurrent illness or patients taking other medications should be carefully adjusted. This is especially important in patients receiving other medications with anticholinergic effects.

***Usage in Geriatrics:*** The use of SINEQUAN on a once-a-day dosage regimen in geriatric patients should be adjusted carefully based on the patient's condition.

***Usage in Pregnancy:*** Reproduction studies have been performed in rats, rabbits, monkeys and dogs and there was no evidence of harm to the animal fetus. The relevance to humans is not known. Since there is no experience in pregnant women who have received this drug, safety in pregnancy has not been established. There has been a report of apnea and drowsiness occurring in a nursing infant whose mother was taking SINEQUAN.

***Usage in Children:*** The use of SINEQUAN in children under 12 years of age is not recommended because safe conditions for its use have not been established.

**Drug Interactions.**

***MAO Inhibitors:*** Serious side effects and even death have been reported following the concomitant use of certain drugs with MAO inhibitors. Therefore, MAO inhibitors should be discontinued at least two weeks prior to the cautious initiation of therapy with SINEQUAN. The exact length of time may vary and is dependent upon the particular MAO inhibitor being used, the length of time it has been administered, and the dosage involved.

***Cimetidine:*** Cimetidine has been reported to produce clinically significant fluctuations in steady-state serum concentrations of various tricyclic antidepressants. Serious anticholinergic symptoms (i.e., severe dry mouth, urinary retention and blurred vision) have been associated with elevations in the serum levels of tricyclic antidepressant when cimetidine therapy is initiated. Additionally, higher than expected tricyclic antidepressant levels have been observed when they are begun in patients already taking cimetidine. In patients who have been reported to be well controlled on tricyclic antidepressants receiving concurrent cimetidine therapy, discontinuation of cimetidine has been reported to decrease established steady-state serum tricyclic anti depressant levels and compromise their therapeutic effects.

***Alcohol:*** It should be borne in mind that alcohol ingestion may increase the danger inherent in any intentional or unintentional SINEQUAN overdosage. This is especially important in patients who may use alcohol excessively.

***Tolazamide:*** A case of severe hypoglycemia has been reported in a type II diabetic patient maintained on tolazamide (1 gm/day) 11 days after the addition of doxepin (75 mg/day).

**Precautions.** Since drowsiness may occur with the use of this drug, patients should be warned of the possibility and cautioned against driving a car or operating dangerous machinery while taking the drug. Patients should also be cautioned that their response to alcohol may be potentiated.

Since suicide is an inherent risk in any depressed patient and may remain so until significant improvement has occurred, patients should be closely supervised during the early course of therapy. Prescriptions should be written for the smallest feasible amount.

Should increased symptoms of psychosis or shift to manic symptomatology occur, it may be necessary to reduce dosage or add a major tranquilizer to the dosage regimen.

**Adverse Reactions. NOTE:** Some of the adverse reactions noted below have not been specifically reported with SINEQUAN use. However, due to the close pharmacological similarities among the tricyclics, the reactions should be considered when prescribing SINEQUAN (doxepin HCl).

*Anticholinergic Effects:* Dry mouth, blurred vision, constipation, and urinary retention have been reported. If they do not subside with continued therapy, or become severe, it may be necessary to reduce the dosage.

*Central Nervous System Effects:* Drowsiness is the most commonly noticed side effect. This tends to disappear as therapy is continued. Other infrequently reported CNS side effects are confusion, disorientation, hallucinations, numbness, paresthesias, ataxia, extrapyramidal symptoms, seizures, tardive dyskinesia, and tremor.

*Cardiovascular:* Cardiovascular effects including hypotension, hypertension, and tachycardia have been reported occasionally.

*Allergic:* Skin rash, edema, photosensitization, and pruritus have occasionally occurred.

*Hematologic:* Eosinophilia has been reported in a few patients. There have been occasional reports of bone marrow depression manifesting as agranulocytosis, leukopenia, thrombocytopenia, and purpura.

*Gastrointestinal:* Nausea, vomiting, indigestion, taste disturbances, diarrhea, anorexia, and aphthous stomatitis have been reported. (See anticholinergic effects.)

*Endocrine:* Raised or lowered libido, testicular swelling, gynecomastia in males, enlargement of breasts and galactorrhea in the female, raising or lowering of blood sugar levels, and syndrome of inappropriate antidiuretic hormone secretion have been reported with tricyclic administration.

*Other:* Dizziness, tinnitus, weight gain, sweating, chills, fatigue, weakness, flushing, jaundice, alopecia, headache, exacerbation of asthma, and hyperpyrexia (in association with chlorpromazine) have been occasionally observed as adverse effects.

*Withdrawal Symptoms:* The possibility of development of withdrawal symptoms upon abrupt cessation of treatment after prolonged SINEQUAN administration should be borne in mind. These are not indicative of addiction and gradual withdrawal of medication should not cause these symptoms.

**Dosage and Administration.** For most patients with illness of mild to moderate severity, a starting daily dose of 75 mg is recommended. Dosage may subsequently be increased or decreased at appropriate intervals and according to individual response. The usual optimum dose range is 75 mg/day to 150 mg/day.

In more severely ill patients higher doses may be required with subsequent gradual increase to 300 mg/day if necessary. Additional therapeutic effect is rarely to be obtained by exceeding a dose of 300 mg/day.

In patients with very mild symptomatology or emotional symptoms accompanying organic disease, lower doses may suffice. Some of these patients have been controlled on doses as low as 25-50 mg/day.

The total daily dosage of SINEQUAN may be given on a divided or once-a-day dosage schedule. If the once-a-day schedule is employed the maximum recommended dose is 150 mg/day. This dose may be given at bedtime. **The 150 mg capsule strength is intended for maintenance therapy only and is not recommended for initiation of treatment.**

Anti-anxiety effect is apparent before the antidepressant effect. Optimal antidepressant effect may not be evident for two to three weeks.

**Overdosage.**

A. Signs and Symptoms

1. Mild: Drowsiness, stupor, blurred vision, excessive dryness of mouth.
2. Severe: Respiratory depression, hypotension, coma, convulsions, cardiac arrhythmias and tachycardias.

Also: urinary retention (bladder atony), decreased gastrointestinal motility (paralytic ileus), hyperthermia (or hypothermia), hypertension, dilated pupils, hyperactive reflexes.

B. Management and Treatment

1. Mild: Observation and supportive therapy is all that is usually necessary.
2. Severe: Medical management of severe SINEQUAN overdosage consists of aggressive supportive therapy. If the patient is conscious, gastric lavage, with appropriate precautions to prevent pulmonary aspiration, should be performed even though SINEQUAN is rapidly absorbed. The use of activated charcoal has been recommended, as has been continuous gastric lavage with saline for 24 hours or more. An adequate airway should be established in comatose patients and assisted ventilation used if necessary. EKG monitoring may be required for several days, since relapse after apparent recovery has been reported. Arrhythmias should be treated with the appropriate antiarrhythmic agent. It has been reported that many of the cardiovascular and CNS symptoms of tricyclic antidepressant poisoning in adults may be reversed by the slow intravenous administration of 1 mg to 3 mg of physostigmine salicylate. Because physostigmine is rapidly metabolized, the dosage should be repeated as required. Convulsions may respond to standard anticonvulsant therapy, however, barbiturates may potentiate any respiratory depression. Dialysis and forced diuresis generally are not of value in the management of overdosage due to high tissue and protein binding of SINEQUAN.

**More detailed professional information available on request.**

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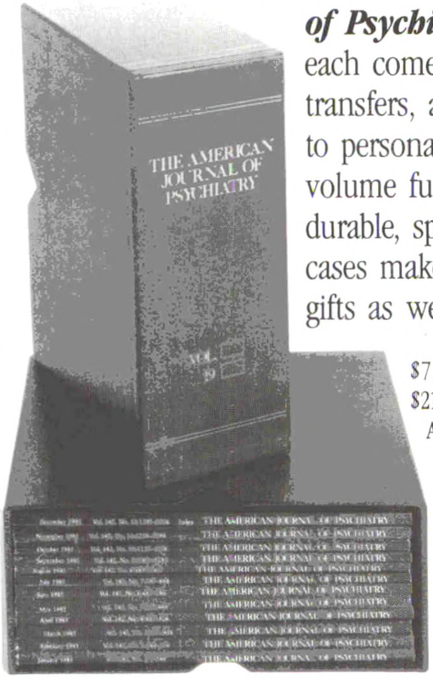
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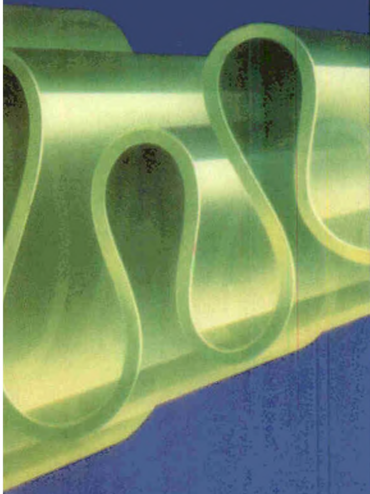

Please see brief summary of Pres[illegible] on next page.

During dose adjustment or episodes of [illegible] of psychotic symptoms, therapy [illegible] HALDOL Decanoate 100 or HAL[illegible] can be supplemented with short-a[illegible] of HALDOL® (haloperidol). The side [illegible] decanoate products are those of HAL[illegible] prolonged action of HALDOL De[illegible] HALDOL Decanoate 50 should be [illegible] management of side effects.

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(HALOPERIDOL) INJECTION 100mg/mL

**HALDOL® Decanoate 50**
(HALOPERIDOL) INJECTION 50mg/mL

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# HALDOL® Decanoate 100

(HALOPERIDOL) INJECTION 100mg/mL

# HALDOL® Decanoate 50

(HALOPERIDOL) INJECTION 50mg/mL

For IM Injection Only

**The following is a brief summary only. Before prescribing, see complete prescribing information in HALDOL and HALDOL Decanoate product labeling.**

**Contraindications:** Since the pharmacologic and clinical actions of HALDOL Decanoate 50 and HALDOL Decanoate 100 are attributed to HALDOL haloperidol as the active medication, Contraindications, Warnings, and additional information are those of HALDOL, modified to reflect the prolonged action.

HALDOL is contraindicated in severe toxic central nervous system depression or comatose states from any cause and in individuals who are hypersensitive to this drug or have Parkinson's disease.

**Warnings:** *Tardive Dyskinesia:* Tardive dyskinesia, a syndrome consisting of potentially irreversible, involuntary, dyskinetic movements may develop in patients treated with antipsychotic drugs. Although the prevalence of the syndrome appears to be highest among the elderly, especially elderly women, it is impossible to rely upon prevalence estimates to predict, at the inception of antipsychotic treatment, which patients are likely to develop the syndrome. Whether antipsychotic drug products differ in their potential to cause tardive dyskinesia is unknown. Both the risk of developing tardive dyskinesia and the likelihood that it will become irreversible are believed to increase as the duration of treatment and the total cumulative dose of antipsychotic drugs administered to the patient increase. However, the syndrome can develop, although much less commonly, after relatively brief treatment periods at low doses. There is no known treatment for established cases of tardive dyskinesia, although the syndrome may remit, partially or completely, if antipsychotic treatment is withdrawn. Antipsychotic treatment, itself, however, may suppress (or partially suppress) the signs and symptoms of the syndrome and thereby may possibly mask the underlying process. The effect that symptomatic suppression has upon the long-term course of the syndrome is unknown. Given these considerations, antipsychotic drugs should be prescribed in a manner that is most likely to minimize the occurrence of tardive dyskinesia. Chronic antipsychotic treatment should generally be reserved for patients who suffer from a chronic illness that 1) is known to respond to antipsychotic drugs, and 2) for whom alternative, equally effective, but potentially less harmful treatments are **not** available or appropriate. In patients who do require chronic treatment, the smallest dose and the shortest duration of treatment producing a satisfactory clinical response should be sought. The need for continued treatment should be reassessed periodically. If signs and symptoms of tardive dyskinesia appear in a patient on antipsychotics, drug discontinuation should be considered. However, some patients may require treatment despite the presence of the syndrome. (For further information about the description of tardive dyskinesia and its clinical detection, please refer to ADVERSE REACTIONS.)

*Neuroleptic Malignant Syndrome (NMS):* A potentially fatal symptom complex sometimes referred to as Neuroleptic Malignant Syndrome (NMS) has been reported in association with antipsychotic drugs. Clinical manifestations of NMS are hyperpyrexia, muscle rigidity, altered mental status (including catatonic signs) and evidence of autonomic instability (irregular pulse or blood pressure, tachycardia, diaphoresis, and cardiac dysrhythmias). Additional signs may include elevated creatine phosphokinase, myoglobinuria (rhabdomyolysis) and acute renal failure. The diagnostic evaluation of patients with this syndrome is complicated. In arriving at a diagnosis, it is important to identify cases where the clinical presentation includes both serious medical illness (e.g., pneumonia, systemic infection, etc.) and untreated or inadequately treated extrapyramidal signs and symptoms (EPS). Other important considerations in the differential diagnosis include central anticholinergic toxicity, heat stroke, drug fever and primary central nervous system (CNS) pathology. The management of NMS should include 1) immediate discontinuation of antipsychotic drugs and other drugs not essential to concurrent therapy, 2) intensive symptomatic treatment and medical monitoring, and 3) treatment of any concomitant serious medical problems for which specific treatments are available. There is no general agreement about specific pharmacological treatment regimens for uncomplicated NMS. If a patient requires antipsychotic drug treatment after recovery from NMS, the potential reintroduction of drug therapy should be carefully considered. The patient should be carefully monitored, since recurrences of NMS have been reported. Hyperpyrexia and heat stroke, not associated with the above symptom complex, have also been reported with HALDOL.

*Usage in Pregnancy:* (see PRECAUTIONS—Usage in Pregnancy) *Combined Use With Lithium:* (see PRECAUTIONS—Drug Interactions)

*General:* Bronchopneumonia, sometimes fatal, has followed use of antipsychotic drugs, including haloperidol. Prompt remedial therapy should be instituted if dehydration, hemoconcentration or reduced pulmonary ventilation occur, especially in the elderly. Decreased serum cholesterol and/or cutaneous and ocular changes have been reported with chemically-related drugs, although not with haloperidol. See PRECAUTIONS—Information for Patients for information on mental and/or physical abilities and on concomitant use with other substances.

**Precautions:** Administer cautiously to patients: (1) with severe cardiovascular disorders, due to the possibility of transient hypotension and/or precipitation of anginal pain (if a vasopressor is required, epinephrine should not be used since HALDOL may block its vasopressor activity and paradoxical further lowering of blood pressure may occur; metaraminol, phenylephrine or norepinephrine should be used); (2) receiving anticonvulsant medications, with a history of seizures, or with EEG abnormalities, because HALDOL may lower the convulsive threshold. If indicated, adequate anticonvulsant therapy should be concomitantly maintained; (3) with known allergies or a history of allergic reactions to drugs; (4) receiving anticoagulants, since an isolated instance of interference occurred with the effects of one anticoagulant (phenindione). Concomitant antiparkinson medication, if required, may have to be continued after HALDOL is discontinued because of different excretion rates; if both are discontinued simultaneously, extrapyramidal symptoms may occur. Intraocular pressure may increase when anticholinergic drugs, including antiparkinson drugs, are administered concomitantly with HALDOL. When HALDOL is used for mania in bipolar disorders, there may be a rapid mood swing to depression. Severe neurotoxicity may occur in patients with thyrotoxicosis receiving antipsychotic medication, including HALDOL.

The 1, 5, 10 mg HALDOL tablets contain FD&C Yellow No. 5 (tartrazine) which may cause allergic-type reactions (including bronchial asthma) in certain susceptible individuals, especially in those who have aspirin hypersensitivity.

*Information for Patients:* Mental and/or physical abilities required for hazardous tasks or driving may be impaired. Alcohol should be avoided due to possible additive effects and hypotension.

*Drug Interactions:* Patients receiving lithium plus haloperidol should be monitored closely for early evidence of neurological toxicity and treatment discontinued promptly if such signs appear. As with other antipsychotic agents, it should be noted that HALDOL may be capable of potentiating CNS depressants such as anesthetics, opiates, and alcohol.

*Carcinogenesis, Mutagenesis and Impairment of Fertility:* No mutagenic potential of haloperidol decanoate was found in the Ames Salmonella microsomal activation assay.

Carcinogenicity studies using oral haloperidol were conducted in Wistar rats (dosed at up to 5 mg/kg daily for 24 months) and in Albino Swiss mice (dosed at up to 5 mg/kg daily for 18 months). In the rat study survival was less than optimal in all dose groups, reducing the number of rats at risk for developing tumors. However, although a relatively greater number of rats survived to the end of the study in high dose male and female groups, these animals did not have a greater incidence of tumors than control animals. Therefore, although not optimal, this study does suggest the absence of a haloperidol related increase in the incidence of neoplasia in rats at doses up to 20 times the usual daily human dose for chronic or resistant patients. In female mice at 5 and 20 times the highest initial daily dose for chronic or resistant patients, there was a statistically significant increase in mammary gland neoplasia and total tumor incidence; at 20 times the same daily dose there was a statistically significant increase in pituitary gland neoplasia. In male mice, no statistically significant differences in incidences of total tumors or specific tumor types were noted.

Antipsychotic drugs elevate prolactin levels; the elevation persists during chronic administration. Tissue culture experiments indicate that approximately one-third of human breast cancers are prolactin dependent *in vitro*, a factor of potential importance if the prescription of these drugs is contemplated in a patient with a previously detected breast cancer. Although disturbances such as galactorrhea, amenorrhea, gynecomastia, and impotence have been reported, the clinical significance of elevated serum prolactin levels is unknown for most patients. An increase in mammary neoplasms has been found in rodents after chronic administration of antipsychotic drugs. Neither clinical studies nor epidemiologic studies conducted to date, however, have shown an association between chronic administration of these drugs and mammary tumorigenesis: the available evidence is considered too limited to be conclusive at this time.

*Usage in Pregnancy:* Pregnancy Category C. Safe use in pregnancy or in women likely to become pregnant has not been established; use only if benefit clearly justifies potential hazards to the fetus.

*Nursing Mothers:* Infants should not be nursed during drug treatment.

*Pediatric Use:* Controlled trials to establish the safety and effectiveness of intramuscular administration in children have not been conducted.

**Adverse Reactions:** Adverse reactions following the administration of HALDOL Decanoate 50 or HALDOL Decanoate 100 are those of HALDOL haloperidol. Since vast experience has accumulated with HALDOL, the adverse reactions are reported for that compound as well as for haloperidol decanoate. As with all injectable medications, local tissue reactions have been reported with haloperidol decanoate.

*CNS Effects: Extrapyramidal Reactions*—Neuromuscular (extrapyramidal) reactions have been reported frequently, often during the first few days of treatment. Generally they involved Parkinson-like symptoms which when first observed were usually mild to moderately severe and usually reversible. Other types of neuromuscular reactions (motor restlessness, dystonia, akathisia, hyperreflexia, opisthotonos, oculogyric crises) have been reported far less frequently, but were often more severe. Severe extrapyramidal reactions have been reported at relatively low doses. Generally, extrapyramidal symptoms are dose-related since they occur at relatively high doses and disappear or become less severe when the dose is reduced. Antiparkinson drugs may be required. Persistent extrapyramidal reactions have been reported and the drug may have to be discontinued in such cases. *Withdrawal Emergent Neurological Signs*—Abrupt discontinuation of short-term antipsychotic therapy is generally uneventful. However, some patients on maintenance treatment experience transient dyskinetic signs after abrupt withdrawal. In certain cases these are indistinguishable from "Tardive Dyskinesia" except for duration. It is unknown whether gradual withdrawal will reduce the occurrence of these signs, but until further evidence is available HALDOL should be gradually withdrawn. *Tardive Dyskinesia*—As with all antipsychotic agents HALDOL has been associated with persistent dyskinesias. Tardive dyskinesia, a syndrome consisting of potentially irreversible, involuntary, dyskinetic movements, may appear in some patients on long-term therapy or may occur after drug therapy has been discontinued. The risk appears to be greater in elderly patients on high-dose therapy, especially females. The symptoms are persistent and in some patients irreversible. The syndrome is characterized by rhythmical involuntary movements of tongue, face, mouth or jaw (e.g., protrusion of tongue, puffing of cheeks, puckering of mouth, chewing movements). Sometimes these may be accompanied by involuntary movements of extremities and the trunk. There is no known effective treatment for tardive dyskinesia; antiparkinson agents usually do not alleviate the symptoms of this syndrome. It is suggested that all antipsychotic agents be discontinued if these symptoms appear. Should it be necessary to reinstitute treatment, or increase the dosage of the agent, or switch to a different antipsychotic agent, this syndrome may be masked. It has been reported that fine vermicular movement of the tongue may be an early sign of tardive dyskinesia and if the medication is stopped at that time the full syndrome may not develop. *Tardive Dystonia*—Tardive dystonia, not associated with the above syndrome, has also been reported. Tardive dystonia is characterized by delayed onset of choreic or dystonic movements, is often persistent, and has the potential of becoming irreversible. *Other CNS Effects*—Insomnia, restlessness, anxiety, euphoria, agitation, drowsiness, depression, lethargy, headache, confusion, vertigo, grand mal seizures, and exacerbation of psychotic symptoms including hallucinations, and catatonic-like behavioral states which may be responsive to drug withdrawal and/or treatment with anticholinergic drugs.

*Body as a Whole:* Neuroleptic malignant syndrome (NMS), hyperpyrexia and heat stroke have been reported with HALDOL. (See WARNINGS for further information concerning NMS.) *Cardiovascular Effects:* Tachycardia, hypotension, hypertension and ECG changes. *Hematologic Effects:* Reports of mild, usually transient leukopenia and leukocytosis, minimal decreases in red blood cell counts, anemia, or a tendency toward lymphomonocytosis; agranulocytosis rarely reported and only in association with other medication. *Liver Effects:* Impaired liver function and/or jaundice. *Dermatologic Reactions:* Maculopapular and acneiform reactions, isolated cases of photosensitivity, loss of hair. *Endocrine Disorders:* Lactation, breast engorgement, mastalgia, menstrual irregularities, gynecomastia, impotence, increased libido, hyperglycemia, hypoglycemia and hyponatremia. *Gastrointestinal Effects:* Anorexia, constipation, diarrhea, hypersalivation, dyspepsia, nausea and vomiting. *Autonomic Reactions:* Dry mouth, blurred vision, urinary retention, diaphoresis, and priapism. *Respiratory Effects:* Laryngospasm, bronchospasm and increased depth of respiration. *Special Senses:* Cataracts, retinopathy and visual disturbances. *Other:* Cases of sudden and unexpected death have been reported in association with the administration of HALDOL. The nature of the evidence makes it impossible to determine definitively what role, if any, HALDOL played in the outcome of the reported cases. The possibility that HALDOL caused death cannot, of course, be excluded, but it is to be kept in mind that sudden and unexpected death may occur in psychotic patients when they go untreated or when they are treated with other antipsychotic drugs.

**IMPORTANT: Full directions for use should be read before HALDOL or HALDOL Decanoate products are administered or prescribed.**

**For information on symptoms and treatment of overdosage, see full prescribing information.**

The short-acting HALDOL injectable form is intended only for acutely agitated psychotic patients with moderately severe to very severe symptoms.

McNeil Pharmaceutical, McNEILAB, INC., Spring House, PA 19477

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**Choosing Partners: Patterns of Romance—How You Select Partners in Intimacy, the Ways You Connect, and Why You Break Apart,** by Martin Blinder, M.D., with Carmen Lynch, M.S.W. Macomb, Ill., Glenbridge Publishing, 1989, 222 pp., $18.95.

**Dreaming With an AIDS Patient,** by Robert Bosnak. Boston, Shambhala (New York, Random House, distributor), 1989, 174 pp., $15.95.

**Stress, Strain, and Vietnam: An Annotated Bibliography of Two Decades of Psychiatric and Social Sciences Literature Reflecting the Effect of the War on the American Soldier. Bibliographies and Indexes in Military Studies 1,** by Norman M. Camp, Robert H. Stretch, and William C. Marshall. New York, Greenwood Press, 1988, 302 pp., $49.95.

**In Her Image: The Unhealed Daughter's Search for Her Mother,** by Kathie Carlson. Boston, Shambhala (New York, Random House, distributor), 1989, 145 pp., $16.95.

**The Encyclopedia of Phobias, Fears and Anxieties,** by Ronald M. Doctor, Ph.D., and Ada P. Kahn. New York, Facts on File, 1989, 476 pp., $40.00.

**Migration and Mental Health in Bahia, Brazil,** by Naomar de Almeida Filho. Salvador, Bahia, Brazil, Caja de Ahorros de la Inmaculada de Aragon, 1987, 179 pp., no price listed (paper).

**Atlas of Electroencephalography,** by Alan Guberman, M.D., C.M., F.R.C.P.(C.), and Madeleine Couture, R.E.T. Boston, Little, Brown and Co., 1989, 216 pp., $145.00 (spiral-bound).

**Cognitive Behaviour Therapy for Psychiatric Problems: A Practical Guide,** edited by Keith Hawton, Paul M. Salkovskis, Joan Kirk, and David M. Clark. New York, Oxford University Press, 1989, 449 pp., $60.00; $24.95 (paper).

**Depression: An Integrative Approach,** edited by Katia R. Herbst, M.A., Ph.D., and Eugene S. Paykel, M.A., M.D. Oxford, Heinemann Medical Books in association with the Mental Health Foundation (Stoneham, Mass., Butterworths, distributor), 1989, 249 pp., $75.00.

**Psychoanalytic Aspects of Fieldwork: Qualitative Research Methods, vol. 18,** by Jennifer C. Hunt. Newbury Park, Calif., Sage Publications, 1989, 91 pp., $12.95; $6.50 (paper).

**Clinical Neurology for Practitioners, 3rd ed.,** by David Myland Kaufman, M.D. Philadelphia, W.B. Saunders Co. (Harcourt Brace Jovanovich), 1990, 513 pp., $70.00.

**Gestalt Therapy: Practice and Theory, 2nd ed.,** by Margaret P. Korb, Jeffrey Gorrell, and Vernon Van De Riet. Oxford, Pergamon Press, 1989, 163 pp., $23.50; $13.95 (paper).

**Perspectives on the AIDS Crisis: Thanatologic Aspects,** edited by Robert S. Lampke, Marcia Fishman, Austin H. Kutscher, Carlo E. Grossi, Roberta Halporn, Leonard M. Liegner, and Esther Chachkes. New York, Foundation of Thanatology, 1989, 138 pp., $15.95 (paper).

**Rating Your Psychotherapist,** by Robert Langs, M.D. New York, Henry Holt and Co., 1989, 284 pp., $17.95.

**Witness to the Fire: Creativity and the Veil of Addiction,** by Linda Schierse Leonard. Boston, Shambhala (New York, Random House, distributor), 1989, 374 pp., $19.95.

**Women and AIDS: A Practical Guide for Those Who Help Others,** by Bonnie Lester. New York, Continuum, 1989, 143 pp., $15.95.

**The Discovery of the Art of the Insane,** by John M. MacGregor. Princeton, N.J., Princeton University Press, 1989, 377 pp., $49.50.

**Dry All Night: The Picture Book Technique That Stops Bedwetting,** by Alison Mack. Boston, Little, Brown and Co., 1989, 174 pp., $17.95.

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**High Times/Low Times: How to Cope With Teenage Depression** (1988), by John E. Meeks, M.D. New York, Berkley Books, 1989, 140 pp., $3.95 (paper).

**The Primitive Edge of Experience,** by Thomas H. Ogden, M.D. Northvale, N.J., Jason Aronson, 1989, 235 pp., $25.00.

**Fear and Courage, 2nd ed.,** by S.J. Rachman. New York, W.H. Freeman and Co., 1990, 393 pp., $32.95; $17.95 (paper).

**XIII Reunion de la Sociedad Española de Psiquiatria Biologica.** Madrid, ARÁN Ediciones, 1988, 671 pp., no price listed (paper).

**Developmental Pathogenesis and Treatment of Borderline and Narcissistic Personalities,** by Donald B. Rinsley, M.D., F.R.S.H. Northvale, N.J., Jason Aronson, 1989, 175 pp., $20.00.

**Alzheimer's Disease: A Practical Guide for Those Who Help Others,** by Judah L. Ronch. New York, Continuum, 1989, 203 pp., $17.95.

**The Disability Management Sourcebook,** by Gail E. Schwartz, M.P.H., Sara D. Watson, M.P.P., Donald E. Galvin, Ph.D., and Else Lipoff. Washington, D.C., Washington Business Group on Health/Institute for Rehabilitation and Disability Management, 1989, 85 pp., $30.00 (paper).

**Couples Counseling: A Practical Guide for Those Who Seek Help,** by John R. Shack. New York, Continuum, 1989, 157 pp., $17.95.

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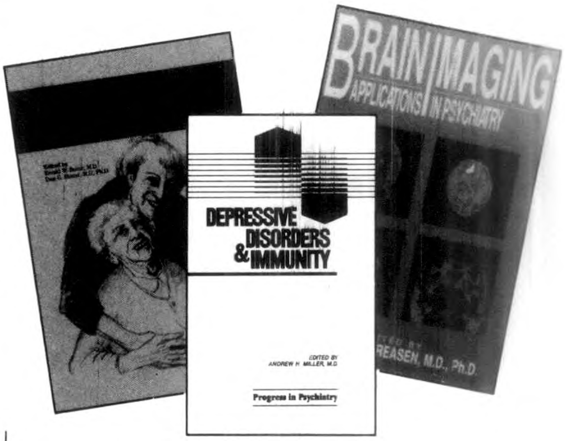

*(Continued from page A12)*

April 29–May 1, 2nd International United Arab Emirates Conference of Psychiatry, Abu Dhabi. Contact Dr. Rafia Ghubash, c/o Dr. Hassan Abd El Rahman, Tawan Hospital, P.O. Box 15258 Al Ain, Abu Dhabi, United Arab Emirates; 677444.

April 30–May 6, annual meeting, American Academy of Neurology, Miami. Contact Jan W. Kolehmainen, Executive Director, 2221 University Avenue, SE, Suite 335, Minneapolis, MN 55414; 612-623-8115.

## MAY

May 3–4, International Congress on Treatment of Mental Illness and Behavioral Disorder in Mentally Retarded Persons, Amsterdam. Contact Netherlands Organization for Postacademic Education in the Social Sciences (PAOS), P.O. Box 325, 2300 AH Leiden, Netherlands; (0)71-278027.

May 4–7, annual meeting, American Federation for Clinical Research, Eastern Section, Washington, DC. Contact Patricia A. McFadden, Account Executive, 6900 Grove Road, Thorofare, NJ 08086; 609-848-1000.

May 5–13, annual meeting, American Psychoanalytic Association, New York. Contact Helen Fischer, Administrative Director, 309 East 49th Street, New York, NY 10017; 212-752-0450.

May 9–13, annual meeting, Society of Biological Psychiatry, New York. Contact David L. Dunner, M.D., Secretary-Treasurer, Harborview Medical Center ZA-15, Seattle, WA 98104; 206-223-3425.

May 10–13, annual meeting, American Association for the History of Medicine, Inc., Baltimore. Contact Arthur J. Viseltear, Ph.D., M.P.H., Secretary-Treasurer, Yale School of Medicine, 333 Cedar Street, New Haven, CT 06510-8015; 203-785-4338.

May 11–13, annual meeting, American Society for Adolescent Psychiatry, New York. Contact David Lewis, Executive Director, 5530 Wisconsin Avenue, NW, Suite 1149, Washington, DC 20815; 301-652-0646.

May 12, annual meeting, American College of Psychoanalysts, New York. Contact Harold Mann, M.D., Secretary General, 2006 Dwight Way, #304, Berkeley, CA 94704; 415-845-7957.

May 12, annual meeting, National Guild of Catholic Psychiatrists, New York. Contact Thomas K. Ciesla, M.D., President, 1301 20th Street, Suite 212, Santa Monica, CA 90404; 213-315-0300.

May 12–13, annual meeting, American Academy of Psychiatrists in Alcoholism and Addictions, New York. Contact Edward Kaufman, M.D., President, P.O. Box 376, Greenbelt, MD 20770; 301-220-0951.

May 12–13, annual meeting, Association for Clinical Psychosocial Research, New York. Contact Gerald Klerman, M.D., President, Payne Whitney Clinic, 525 East 68th Street, New York, NY 10021; 617-746-3675.

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May 12–17, annual meeting, Christian Medical and Dental Society, Psychiatry Section, New York. Contact Don Gent, M.D., President, P.O. Box 830689, Richardson, TX 75083-0689; 214-783-8384.

May 12–17, 143rd Annual Meeting of the American Psychiatric Association, New York. Contact Cathy Earnest-Nash, Office to Coordinate the Annual Meeting, APA, 1400 K Street, NW, Washington, DC 20005; 202-682-6237.

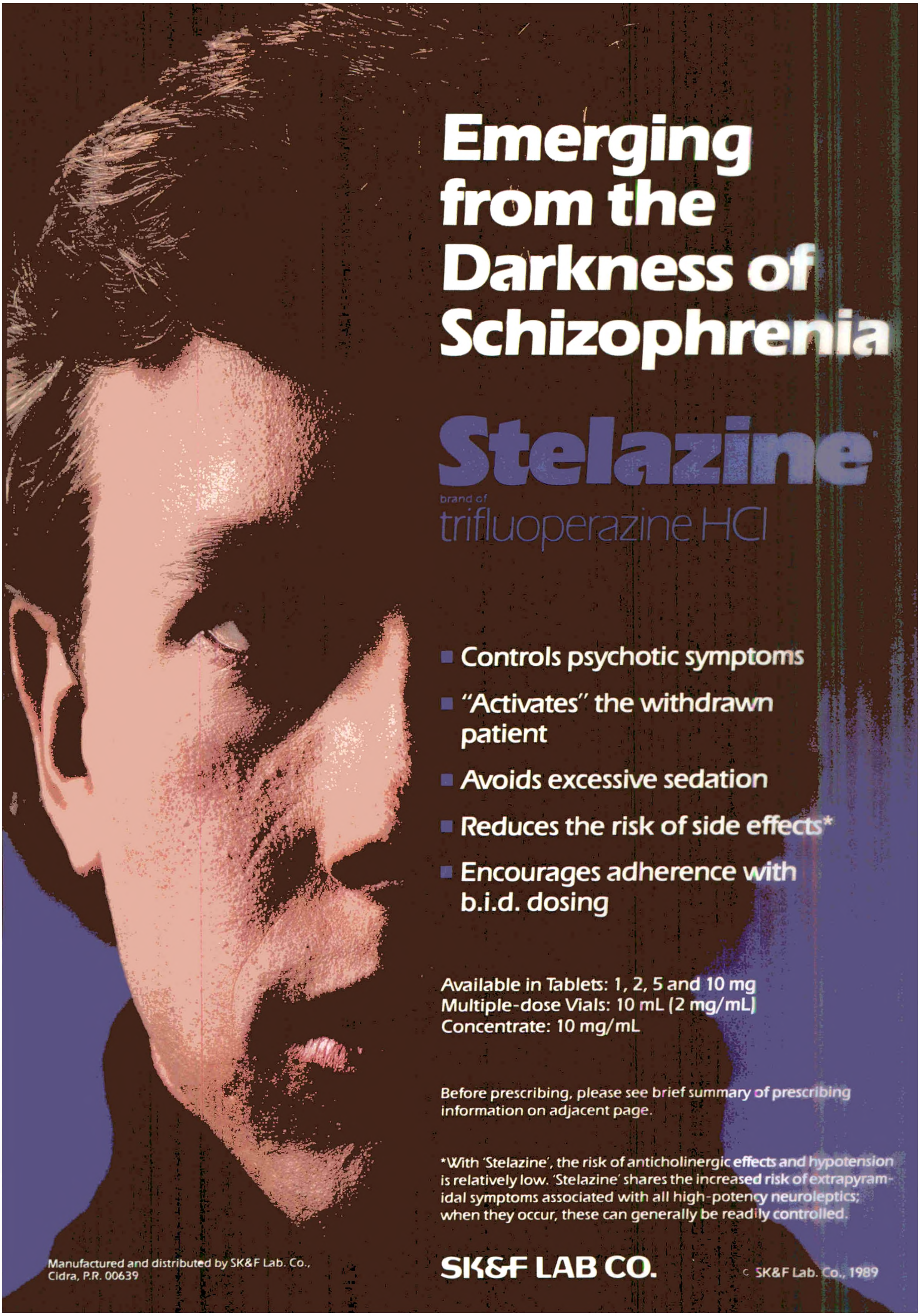
May 17–29, annual meeting, American Geriatrics Society, Atlanta. Contact Linda Hiddemen Barondess, Executive Vice-President, 770 Lexington Avenue, Suite 400, New York, NY 10021; 212-308-1414.

May 19, annual meeting, Recovery, Incorporated (The Association of Nervous and Former Mental Patients), Chicago. Contact Mary Jane Maggio, Executive Director, 802 North Dearborn Street, Chicago, IL 60610; 312-337-5661.

May 22–24, 2nd World Congress on Chronic Rhonchopathy, Barcelona. Contact Secretaria Tecnica, BRP Barcelona Relaciones Publicas, Edificio Layetana, Calle Pau Claris, n. 138, 7o 4o, 08009 Barcelona, Spain; 93-215-7214.

May 22–25, regional symposium, World Psychiatric Association, Hong Kong. Contact Dr. C.M. Chung, 611 Melbourne Plaza, Queen's Road, Central Hong Kong, China.

May 24–25, "Day Treatment of Children," The Clarke Institute of Psychiatry, Child and Family Studies Centre, Toronto. Contact Thomas Yoannidis, Clarke Institute of Psychiatry, 250 College Street, Toronto, Ontario, Canada, M5T 1R8; 416-979-2221, ext. 2260.



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**Contraindications:** Comatose or greatly depressed states due to C.N.S. depressants, blood dyscrasias; bone marrow depression; liver damage.

**Warnings:** Tardive dyskinesia (TD) may develop in patients treated with neuroleptic (antipsychotic) drugs. The risk of TD and likelihood of irreversibility are thought to increase as duration of treatment and total cumulative neuroleptic dose increase. Much less commonly, the syndrome can develop after relatively brief treatment at low doses. There is no known treatment for TD, although it may remit if neuroleptics are withdrawn. Neuroleptic treatment may suppress signs and symptoms of the syndrome and thereby mask the underlying disease process. To minimize risk of TD, generally reserve chronic neuroleptic treatment for patients who suffer from chronic illness that responds to neuroleptics and for whom alternative, effective, less harmful treatments are not available or appropriate. In patients requiring chronic treatment, the minimal effective dose and shortest duration of treatment should be sought. Periodically reassess need for continued treatment. If signs and symptoms of TD appear, discontinuation of neuroleptics should be considered. (See PRECAUTIONS.)

Neuroleptic Malignant Syndrome (NMS), a potentially fatal symptom complex, has been reported in association with antipsychotic drugs. Clinical manifestations include: Hyperpyrexia, muscle rigidity, altered mental status and evidence of autonomic instability.

The management of NMS should include 1) immediate discontinuation of antipsychotic drugs and other drugs not essential to concurrent therapy, 2) intensive symptomatic treatment and medical monitoring, and 3) treatment, if available, of any concomitant serious medical problems.

'Stelazine' Concentrate contains sodium bisulfite, which may cause allergic-type reactions including anaphylactic symptoms or asthmatic episodes in certain susceptible people. The prevalence of sulfite sensitivity in the general population is unknown and probably low and is seen more frequently in asthmatic than in non-asthmatic people.

Generally avoid using in patients hypersensitive (e.g., have had blood dyscrasias, jaundice) to any phenothiazine. Caution patients about activities requiring alertness (e.g., operating vehicles or machinery), especially during the first few days' therapy. Additive depressant effect is possible with other C.N.S. depressants, including alcohol. Do not use in pregnancy except when essential and potential benefits clearly outweigh possible hazards. Prolonged jaundice, extrapyramidal signs, hyperreflexia and hyporeflexia have been reported in newborns whose mothers received phenothiazines. There is evidence that phenothiazines are excreted in the breast milk of nursing mothers.

**Precautions:** Since some patients chronically exposed to neuroleptics will develop tardive dyskinesia, it is advised that, if possible, full information about this risk be given to patients or their guardians when chronic use is contemplated.

Use cautiously in angina. Avoid high doses and parenteral use when cardiovascular system is impaired since hypotension has occurred. Antiemetic effect may mask the signs of overdosage of other drugs or obscure diagnosis and treatment of certain physical disorders. Prolonged use of high doses may result in cumulative effects with severe C.N.S. or vasomotor symptoms. If retinal changes occur, discontinue drug. Agranulocytosis, thrombocytopenia, pancytopenia, anemia, cholestatic jaundice, liver damage have been reported. Use cautiously in patients with glaucoma.

Patients with a history of long-term therapy with 'Stelazine' and/or other neuroleptics should be evaluated periodically for possible dosage adjustment or discontinuance of drug therapy. Neuroleptic drugs cause elevated prolactin levels that persist during chronic use. Since approximately one-third of human breast cancers are prolactin-dependent in vitro, this elevation is of potential importance if neuroleptic drug use is contemplated in a patient with a previously detected breast cancer. However, clinical and epidemiologic studies to date have not shown an association between the chronic use of neuroleptic drugs and mammary tumorigenesis. Chromosomal aberrations in spermatocytes and abnormal sperm have been demonstrated in rodents treated with certain neuroleptics. Use cautiously in persons who will be exposed to extreme heat.

Phenothiazines may diminish the effect of oral anticoagulants. Phenothiazines can produce alpha-adrenergic blockade. Concomitant use of phenothiazines with propranolol increases plasma levels of both drugs. Concurrent use of phenothiazines may counteract antihypertensive effects of guanethidine and related compounds. Thiazide diuretics may accentuate the orthostatic hypotension that may occur with phenothiazines. Phenothiazines may lower the convulsive threshold and may also precipitate phenytoin toxicity; dosage adjustments of anticonvulsants may be necessary. If neuromuscular reactions occur in pregnant women, or in children, permanently stop neuroleptic therapy. Patients should not receive 'Stelazine' 48 hours before or 24 hours after myelography with the contrast medium metrizamide. The presence of phenothiazines may produce false positive phenylketonuria (PKU) test results.

**Adverse Reactions:** Drowsiness, dizziness, skin reactions, rash, dry mouth, insomnia, amenorrhea, fatigue, muscular weakness, anorexia, lactation, blurred vision. Neuromuscular (extrapyramidal) reactions: motor restlessness, dystonias, pseudo-parkinsonism, tardive dyskinesia, and a variant, tardive dystonia.

**Other adverse reactions reported with Stelazine (trifluoperazine HCl, SK&F) or other phenothiazines:** Some adverse effects are more frequent or intense in specific disorders (e.g., mitral insufficiency or pheochromocytoma).

Grand mal and petit mal convulsions, particularly in the presence, or with history, of EEG abnormalities; altered cerebrospinal fluid proteins; cerebral edema; prolongation and intensification of the action of C.N.S. depressants, atropine, heat, and organophosphorus insecticides; nasal congestion, headache, nausea, constipation, obstipation, adynamic ileus, ejaculatory disorders/impotence, priapism, atonic colon, urinary retention, miosis and mydriasis; reactivation of psychotic processes, catatonic-like states, hypotension (sometimes fatal); cardiac arrest; leukopenia, eosinophilia, pancytopenia, agranulocytosis, thrombocytopenic purpura, hemolytic anemia, aplastic anemia, jaundice, biliary stasis, hyperglycemia, hypoglycemia, glycosuria, menstrual irregularities, galactorrhea, gynecomastia, false positive pregnancy tests, photosensitivity, itching, erythema, urticaria, eczema up to exfoliative dermatitis, asthma, laryngeal edema, angioneurotic edema, anaphylactoid reactions, peripheral edema; reversed epinephrine effect; hyperpyrexia; mild fever after large I.M. doses; increased appetite; increased weight; a systemic lupus erythematosus-like syndrome; pigmentary retinopathy; with prolonged administration of substantial doses, skin pigmentation, epithelial keratopathy, and lenticular and corneal deposits; neuroleptic malignant syndrome, which may be fatal; EKG changes—particularly nonspecific, usually reversible Q and T wave distortions—have been observed. Temporary nausea, vomiting, dizziness, and tremulousness may follow abrupt cessation of high-dose therapy. NOTE: Sudden death in patients taking phenothiazines (apparently due to cardiac arrest or asphyxia due to failure of cough reflex) has been reported.

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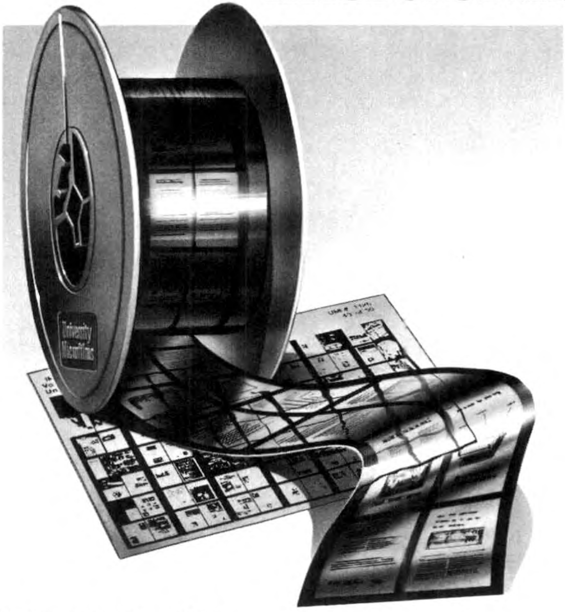

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**Before prescribing, please consult complete product information, a summary of which follows:**

**INDICATIONS:** Management of anxiety disorders, or short-term relief of symptoms of anxiety. Anxiety or tension associated with the stress of everyday life usually does not require treatment with an anxiolytic. Symptomatic relief of acute agitation, tremor, delirium tremens and hallucinosis due to acute alcohol withdrawal; adjunctively in skeletal muscle spasm due to reflex spasm to local pathology; spasticity caused by upper motor neuron disorders; athetosis; stiff-man syndrome; convulsive disorders (not as sole therapy).

The effectiveness of Valium in long-term use, that is, more than 4 months, has not been assessed by systematic clinical studies. The physician should periodically reassess the usefulness of the drug for the individual patient.

**CONTRAINDICATED:** Known hypersensitivity to the drug. Children under 6 months of age. Acute narrow angle glaucoma; may be used in patients with open angle glaucoma who are receiving appropriate therapy.

**WARNINGS:** Not of value in psychotic patients. Caution against hazardous occupations requiring complete mental alertness. When used adjunctively in convulsive disorders, possibility of increase in frequency and/or severity of grand mal seizures may require increased dosage of standard anticonvulsant medication; abrupt withdrawal may be associated with temporary increase in frequency and/or severity of seizures. Advise against simultaneous ingestion of alcohol and other CNS depressants.

***Usage in Pregnancy:* Use of minor tranquilizers during first trimester should almost always be avoided because of increased risk of congenital malformations as suggested in several studies. Consider possibility of pregnancy when instituting therapy; advise patients to discuss therapy if they intend to or do become pregnant.**

Withdrawal symptoms of the barbiturate type have occurred after discontinuation of benzodiazepines (see Drug Abuse and Dependence).

**PRECAUTIONS:** If combined with other psychotropics or anticonvulsants, consider carefully pharmacology of agents employed; drugs such as phenothiazines, narcotics, barbiturates, MAO inhibitors and other antidepressants may potentiate its action. Usual precautions indicated in patients severely depressed, or with latent depression, or with suicidal tendencies. Observe usual precautions in impaired renal or hepatic function. Limit dosage to smallest effective amount in elderly and debilitated to preclude ataxia or oversedation.

The clearance of Valium and certain other benzodiazepines can be delayed in association with Tagamet (cimetidine) administration. The clinical significance of this is

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unclear. Inform patients to consult physician before increasing dose or abruptly discontinuing diazepam.

**SIDE EFFECTS:** Drowsiness, confusion, diplopia, hypotension, changes in libido, nausea, fatigue, depression, dysarthria, jaundice, skin rash, ataxia, constipation, headache, incontinence, changes in salivation, slurred speech, tremor, vertigo, urinary retention, blurred vision. Paradoxical reactions such as acute hyperexcited states, anxiety, hallucinations, increased muscle spasticity, insomnia, rage, sleep disturbances, stimulation have been reported; should these occur, discontinue drug. Isolated reports of neutropenia, jaundice; periodic blood counts and liver function tests advisable during long-term therapy.

*Drug Abuse and Dependence:* Withdrawal symptoms similar to those noted with barbiturates and alcohol have occurred following abrupt discontinuation of diazepam, more severe seen after excessive doses over extended periods; milder after taking continuously at therapeutic levels for several months. After extended therapy, avoid abrupt discontinuation and taper dosage. Carefully supervise addiction-prone individuals because of predisposition to habituation and dependence.

**DOSAGE:** Individualize for maximum beneficial effect. *Adults:* Anxiety disorders, symptoms of anxiety, 2 to 10 mg b.i.d. to q.i.d.; alcoholism, 10 mg t.i.d. or q.i.d. in first 24 hours, then 5 mg t.i.d. or q.i.d. as needed; adjunctively in skeletal muscle spasm, 2 to 10 mg t.i.d. or q.i.d.; adjunctively in convulsive disorders, 2 to 10 mg b.i.d. to q.i.d. *Geriatric or debilitated patients:* 2 to 2½ mg, 1 or 2 times daily initially, increasing as needed and tolerated (See Precautions.) *Children:* 1 to 2½ mg t.i.d. or q.i.d. initially, increasing as needed and tolerated (not for use under 6 months).

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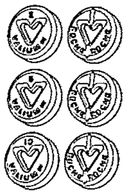

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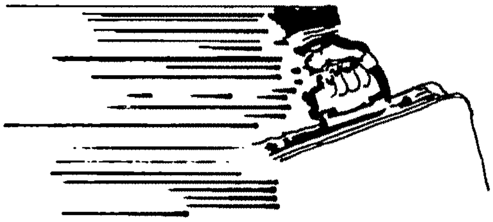

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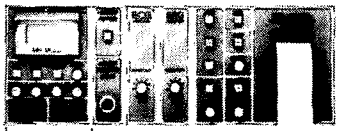

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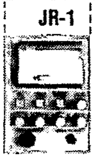

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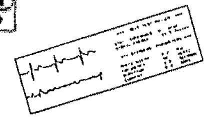

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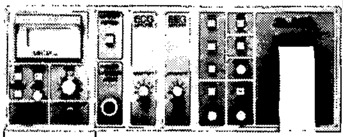

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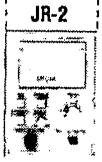

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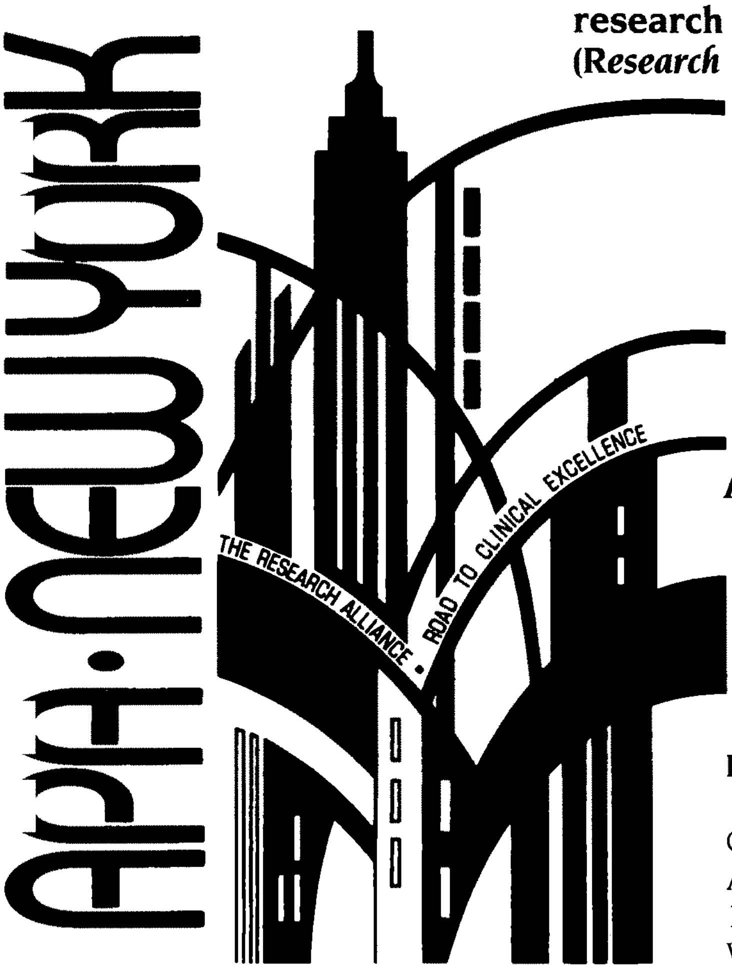
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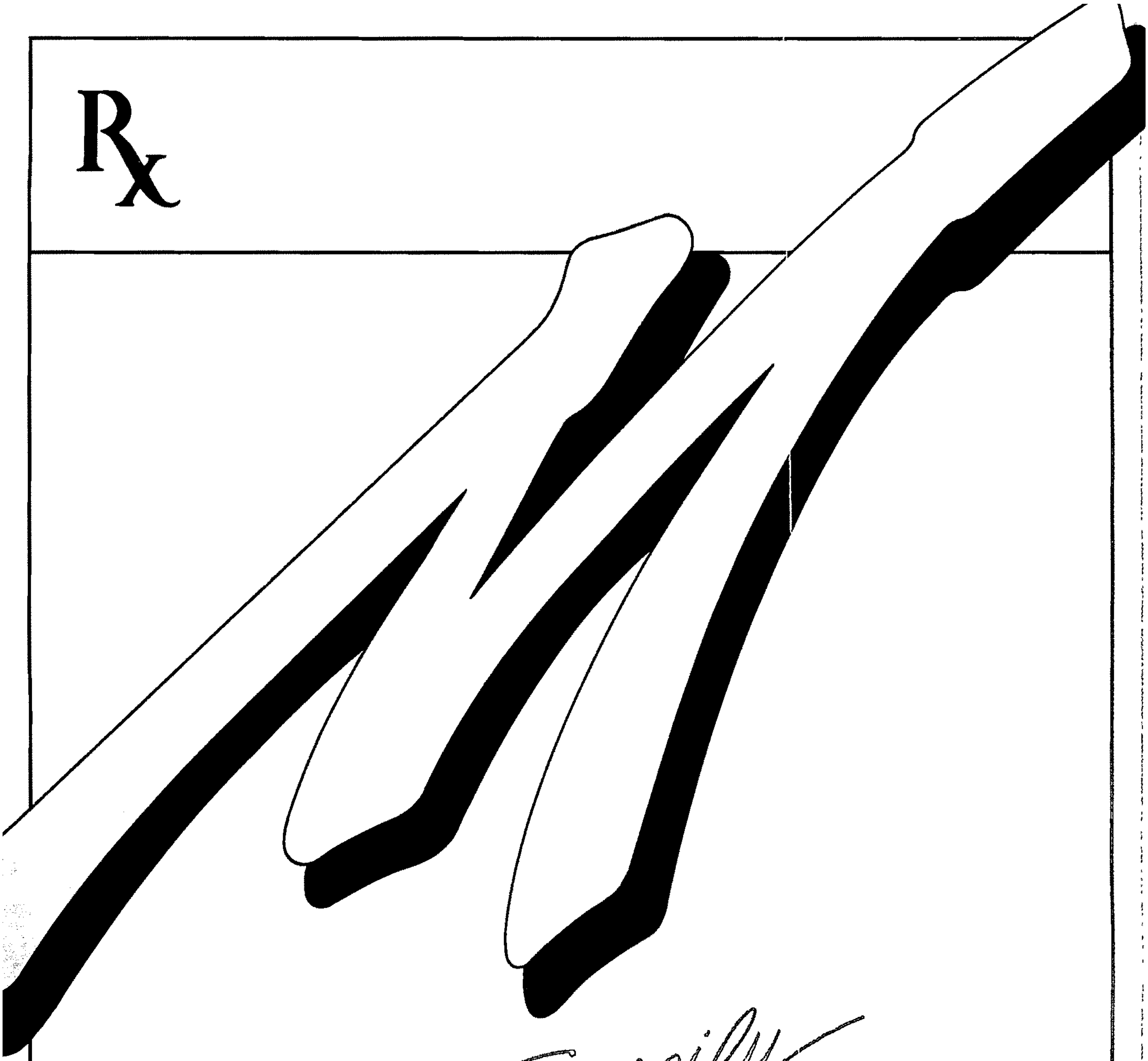

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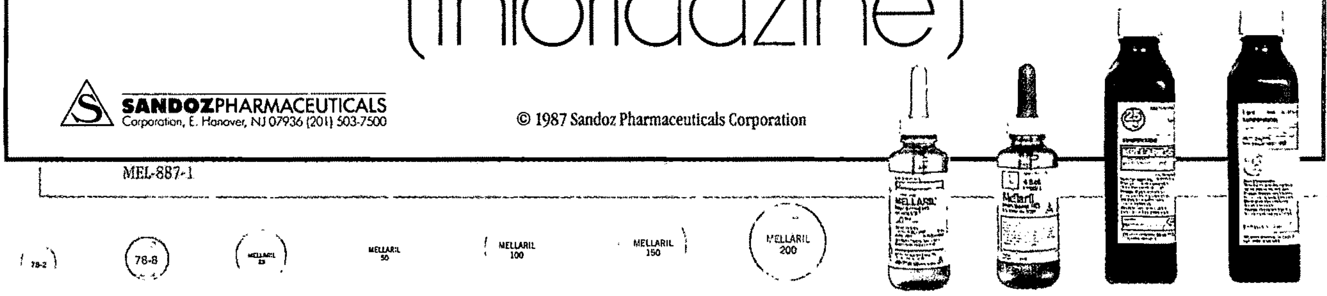

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THE AMERICAN JOURNAL OF PSYCHIATRY
*Special Articles*

# Toward a Clinical Model of Psychotherapy for Depression, I: Systematic Comparison of Three Psychotherapies

**T. Byram Karasu, M.D.**

*In a two-part series, the author explores the current status of psychotherapy for depression. In part I, three predominant approaches to the psychological treatment of depressive disorders today—psychodynamic, cognitive, and interpersonal—are described and contrasted schematically. They are depicted as conceptually different but potentially complementary with regard to 1) basic characteristics, including theoretical orientation, major strategies, goals, and mechanisms of change, and 2) respective advantages and limitations. This clinical comparison forms the foundation of an integrative and selective model for the treatment of depression.*

(Am J Psychiatry 1990; 147:133–147)

From the 1930s to 1960s, the predominant therapies for major affective disorders were physical treatments and, of more controversial utility, traditional psychoanalysis (1). However, in the last two decades various psychosocial modalities have been increasingly used (with or without pharmacotherapy), and, perhaps equally crucial, their efficacy has been subjected to rigorous scientific study, which previously had been unavailable or inadequate (2). In particular, several new interventions, many short-term, have been expressly designed for depressive disorders (e.g., cognitive therapy, interpersonal therapy) or adapted to them (e.g., psychoanalytic or dynamic therapies) (3–7).

This increase in investigation has resulted in a wide array of psychological interventions, which are now part of the total treatment armamentarium for depression (8). While certain forms of depressive illness (e.g., bipolar mood disorder) still respond much better to somatic approaches (e.g., lithium), other types of depressive psychopathology can be successfully treated by psychological means (9). As in the larger field of psychiatry, however, pioneering descriptions of these options have typically tended to portray only one modality or approach and to involve only the form originated and/or preferred by its proponents. Despite increasing efforts to take a broader look at the current alternatives (10–12), such studies may be limited to a single basic contrast, such as psychoanalytic versus cognitive therapy (11), or may be incomplete—leaving direct comparisons implicit or not examining treatment that borrows central elements from different approaches (13).

The two papers in this series are intended to begin to fill these two gaps. In this article I will compare, on a variety of theoretical and technical dimensions, the three predominant psychotherapeutic approaches to depression today: psychodynamic, cognitive/behavioral, and interpersonal. In the second paper, which will appear next month, I will use these comparisons as the foundation for a treatment model that draws on both unique and shared elements of several perspectives.

## PSYCHODYNAMIC APPROACH

### *Concepts of Pathology and Etiology*

The core conceptualizations of the etiology and pathogenesis of depression within a psychodynamic

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framework are rooted in Freud's general personality theories of infantile sexuality and intrapsychic conflict (14) and closely parallel some of the subsequent trends in overall psychoanalytic thinking (i.e., from instinct theory to ego and self psychology). In orthodox terms, depressive symptoms were originally viewed as a blockage of libido: when one is obliged to give up one's sexual aim without being gratified, he feels unloved and incapable of loving; consequently he despairs of himself and his future (15). Also observed in depressed patients was the same kind of ambivalence Freud (16) had earlier found in obsessional neurotic patients, in which hostility interferes with the capacity to love. A model of regression based on Freud's stages of psychosexual development was likewise applied to depression; unresolved conflict at the oral phase was considered directly related to the excessive need and subsequent search for oral gratification and to an unconscious wish to destroy (i.e., devour) the desired but frustrating sexual object (17).

An extension of his work on narcissism (18), the classic Freudian treatise specifically on depression is "Mourning and Melancholia" (19), which compares normal grief with pathological depression. The former is regarded as a reaction to the loss of an external object (i.e., actual death), whereas in the melancholic patient "the object has not perhaps actually died but has been lost as an object of love." The major intrapsychic consequence is an impoverished ego insofar as it becomes identified with the lost object. For Freud there were thus "three preconditions of melancholia—loss of the object, ambivalence, and regression of libido into the ego." In short, the person's anger and disappointment are turned inward toward himself instead of toward the real object, for whom his aggression is meant; it is presumed that henceforth a repressed rage (aggressive cathexes in place of libidinal cathexes) underlies the depressed affect. On the basis of traditional psychoanalytic theory, Abraham (20) gradually formulated five factors in the pathogenesis of melancholia: a constitutional overemphasis on oral eroticism, fixation of psychosexual development at the oral stage, early and repeated childhood disappointments in love, occurrence of first major developmental disappointment before oedipal wishes are resolved, and repetition of primary disappointment in later life. Further tracing the theme of separation and loss (both real and perceived), later studies of acute grief in adults (21, 22) have confirmed Freud's observations and the many features that grief shares with pathological depression; they also highlight significant symptoms not seen in normal bereavement, including functional impairment, suicidal ideation, and overwhelming feelings of worthlessness (23).

Subsequent dynamic theory largely shifted to the importance of object relations and development of self, especially the issues involving self-esteem and its determinants. As a conceptual bridge toward psychological predisposition (rather than constitution), Rado (24) stressed the dependence of the depressive person's self-esteem on narcissistic supplies outside the self, describing the motive as a "great despairing cry for love." Klein (25) hypothesized a period of great ambivalence called "the depressive position," marked not only by fear of loss of love but by guilt about desire for the hated object, which if not resolved predisposes the child to later depression. Fenichel (26) suggested that the depressive person sustained a narcissistic injury in early childhood (i.e., traumatic disappointment in parental affection) whereby self-esteem and love became equated and that the entire depressive process is an attempt to repair the damaged ego. Bibring's radical view of depression (27), as a fundamental ego state, involved consolidation of all depressive phenomena into a loss of self-esteem, and he postulated that different unresolved psychosexual stages lead to different types of depression. Thenceforth, the theoretical tide has increasingly turned away from psychoanalytic metapsychology to notions of depression as a basic affect, and from loss of a love object to the more global erosion of a sense of well-being (28).

### *Current Directions*

In her more than 25 years of work with the ego psychology of depressive persons, Jacobson (29) has established loss of self-esteem as their central psychological problem and exaggerated dependency as a specific ego weakness, and she has carefully examined the nature of ego regression in the depressive patient by delineating several intrapsychic determinants of this fragile self-esteem: superego impairment (very harsh), faulty ego ideal (unrealistic or grandiose idealized love objects), pathological development of self-representations (devalued or distorted body image), immature and self-critical ego functions, and, in severe pathology, the dissolution of all these structures. Kohut's theories on the formation and restoration of the self (30, 31), albeit not directed primarily at depressive illness, have placed in bold relief the need for empathic self-objects in the development of normal self-esteem and the impact of early attachment issues on later problems in separation-individuation. He suggested that when the self is seriously damaged or destroyed, the child turns away from unempathic or absent self-objects to escape depression. Deprivation of idealized self-objects, for example, can result in "empty" depression (depletion of self-esteem and vitality) or "guilt" depression (uncurbed self-rejection and self-blame).

Current theoretical concepts incorporate some of the classic and later ego analytic and self constructs. Like other psychopathology, depression is considered the consequence of underlying conflict, and emphasis is placed on the influence of the past on present object relationships—specifically, excessive reliance on limited external sources of gratification for a sense of worth. In regard to the latter, Arieti (32) discerned two basic patterns of depressive personality organization—"dominant other" (the depressive person relies solely on another person) and "dominant goal" (the external source of esteem is the fulfillment of some great ambition). Both types are founded on the childhood development of a maladaptive way of bolstering the sense of self (27).

In summary, modern dynamic theory now combines, to greater or lesser degrees, such psychoanalytic formulations as early childhood disappointment and loss (which predispose to later depression), damaged self-esteem arising from a marked discrepancy between the actual self and ego ideal, persistence of narcissistic rage beneath an unloved and punished self, omnipotent wishes that both tenuously support and defensively fend off a sense of helplessness and hopelessness, and difficulties in autonomy and intimacy due to reactivation of intrapsychic conflicts about these unsettled issues arising in infancy (33). This largely unconscious matrix forms the foundation for subsequent depressive episodes through repetition of childhood experiences with significant others; this reiteration of earlier patterns is manifested in a breakdown of the intrapsychic processes that maintain self-esteem. These theoretical assumptions have remained essentially intact despite revisions of the concepts regarding the precise nature of unresolved remnants from childhood that are carried to adulthood (i.e., historically, these remnants were initially attributed to repressed real events, subsequently to forbidden fantasies, and most recently, to persistent erroneous beliefs) (3). Moreover, these assumptions continue to underlie current dynamic treatment, despite significant technical differences between long-term and short-term modalities (33).

### *Primary Tools and Practices*

Three background issues are relevant to the use of psychodynamic techniques in depression.

1. Psychodynamic techniques, derived from psychoanalysis, were originally developed for general application to neurotic personality structure, not for treating specific depressive symptoms. Thus, direct applications to major depression have been relatively sparse (3, 29, 34).
2. Because the psychoanalytic approach has evolved over nearly a century, it now encompasses a varied spectrum of schools and strategies, ranging from classical open-ended formats (35) to contemporary time-limited ones (36–39) and including modifications that are both extrinsic (e.g., reduced frequency) and intrinsic (e.g., greater emphasis on the here-and-now) (40, 41).
3. Because of the historical variations in individual schools and techniques and the long-standing difficulties in standardization of the art of analysis, dynamic practices have only begun to be defined and operationalized in treatment manuals (6, 7).

The primary psychodynamic strategies are insight-oriented and include confrontation (evocative questioning), clarification (elaboration or sharper focus), interpretation (the sine qua non of dynamic treatment: assignment of underlying meaning or cause to a feeling or behavior), and working through (continual integration of the entire interpretive process). These techniques are essentially designed to facilitate analysis of transference and resistance—exploration of the ongoing therapist-patient relationship and obstacles to it by means of projecting past positive and negative feelings toward significant figures onto the current interpersonal situation (35). Luborsky's principles of psychoanalytic psychotherapy (7) are based on the need to formulate and reformulate the patient's main relationship problems in the context of the underlying transference relationship so as to derive a core conflictual relationship theme; this motif covers all three of the patient's relationship spheres: past, current in-treatment, and current out-of-treatment. Strupp and Binder's time-limited dynamic psychotherapy (6) uses a "focal narrative" to address repeated problems of living based on real or imagined interpersonal transactions.

Recent descriptions of the changes in psychodynamic treatment theory and practice since Freud's time portray a spectrum of expressive and supportive techniques, although traditionally they have been regarded as antithetical (41). Strupp et al. (33) have suggested that while the underlying assumptions are identical, modern techniques differ from traditional dynamic practices in three major ways: 1) shorter treatment duration, the crucial factor, which is often a direct function of the depth or extent of therapist goals (symptomatic versus characterological change), 2) a more active role on the part of the therapist (direct versus reflective stance), and 3) a more vigorous approach (confronting defenses and clarifying present problems versus interpreting core conflicts). Specific treatment variations include Sifneos's short-term anxiety-provoking psychotherapy (36), which, like long-term analysis, focuses on original oedipal conflict and uses transference interpretations as its major tool; Davanloo's highly confrontational approach (38), in which transference is interpreted in terms of childhood experiences and therapist-parent links are made but the primary modus operandi is persistent challenge of defensive behaviors involved in the patient's resistance to human alliance; and Mann's time-limited psychotherapy (37), which uses a pre-set finite period in which to examine preoedipal and oedipal development in terms of the patient's unconscious experience of time.

The application of psychodynamic techniques to treatment of depression entails careful examination, within an essentially closed dyadic system, of the depressed patient's unrealistic responses to the therapist as the patient replays early disappointment in parental affection, attempts to gain lost love, and makes specific self-protective maneuvers that obstruct therapeutic progress. Particular ego distortions (e.g., excessive ego ideals) and superego defects (e.g., unduly harsh conscience) are the structural intrapsychic foci for exploration (29). Especially in the initial phase of treatment, the therapist may confront defenses and pathological patterns of behavior (e.g., idealization, manipulativeness, clinging dependency) in the depressive patient's attempts to gain magical relief and reinstate self-esteem (42). In fact, many now believe that confrontation of negative transference is essential from the very beginning (6, 36, 38). Using a nonanalytic measure, the dynamic therapist may also encourage cathartic release of repressed aggressive affect, which is presumed to underlie the depressive disorder (43). This method does not directly facilitate insight but can be at least temporarily therapeutic, since anger is expressed toward the therapist as a substitute for early frustrating figures. Recent clinical observations indicate that short-term psychodynamic strategies for depression may also vary but have in common four successive stages of treatment (34).

1. During *primary resistance* to the formation of a therapeutic alliance, in which the depressed patient is fending off primary loss in response to early parental separation, the therapist may challenge and clarify the patient's unresolved ambivalence toward his parents.
2. During *treatment resistance,* the beginning of defensive reactions against the therapy process itself, the therapist continually interprets the depressive patient's repeated self-defeating behavior and fears of retaliation.
3. During *termination resistance,* in which the patient starts to sense impending separation from the therapist and remobilizes earlier irrational reactions to loss, the therapist often must deal with the open expression of anger.
4. By *termination resolution*—the depressed patient's relatively realistic grief over the loss of the therapist—therapist techniques are consolidated in a continual process of working through core conflicts by means of resolving current ones, both within and outside the therapy sessions.

### *Therapeutic Relationship and Therapist Role*

The formation of a transferential relationship to explore unconscious repetition of defensive and adaptive coping patterns formed in the past is the hallmark of the dynamic approach. Brief dynamic therapies are based on a modified transference paradigm (33), in which the current therapeutic relationship is an in vivo expression of the patient's problems with relatedness. The establishment of a trusting working alliance (33) for realistic interaction between partners is the foundation of the ensuing transference process. Here the therapist's major role is as an interpreter/reflector (44); this role includes such features as a primarily receptive attitude (principle of evenly suspended attention), neutral acceptance ("blank screen"), and relative frustration (rule of abstinence) (35). These practices have altered, however, and are now more flexible, especially in terms of the therapist's directness and activity (6). Therapist silence, classically used to facilitate free association and regression, may be applied occasionally to encourage transference formation in attempts to tap more repressed material. This practice is embedded in receptive listening, which prevails throughout treatment.

Luborsky (7) delineated the dynamic therapist's expressive-supportive role. The expressive aspect has four phases: the therapist listens receptively, understands, responds, and returns to listening while bearing in mind the patient's reaction to his previous response. The basic attitude is expectant and involves both observing and experiencing (33), which requires that the therapist be acutely attentive to the patient so that he can resonate with the patient's feelings and be aware of his own emotions. The supportive stance involves maintaining the patient's experience of a helping alliance by conveying empathy and nonjudgmental respect for the patient and by communicating realistic hope. These therapist attitudes are the means for establishing a therapeutic alliance and transference relationship of benign dependency, through which positive and negative transference and extratransference manifestations are confronted, clarified, and worked through in the here-and-now.

### *Major Goals and Mechanisms of Change*

Belief in insight as the primary psychodynamic mechanism of change is based on the philosophy that the unexamined life repeats itself; the patient returns to more regressed patterns of behavior as long as unconscious intrapsychic conflicts remain repressed—unremembered, unrevealed, and therefore unresolved (45). The depressive patient's response to past experiences of loss or failure is unexpressed feelings related to his injured ego (repressed hostility, ambivalence toward significant others), which persist until he gains understanding and works through narcissistic cravings for love (29). The symptoms of depression are thought to subside as the patient brings to the surface his pervasive disappointment in parental affection and approval stemming from childhood or, in shorter-term approaches, as the patient comprehends scenarios within treatment that reiterate comparable current relations to significant others (3, 6, 7). In particular, the depressed patient is helped to recognize the latent meaning of his special vulnerability to loss of self-esteem and the excessiveness of his demands, which are related to pervasive feelings of sadness, guilt, and unworthiness (29). Of course, this process occurs within the context of a transferential and empathic relationship between therapist and patient, in which the therapist becomes a role model who represents both an old and new object (46).

In addition, as the patient recounts early or recent memories and experiences, he can consciously examine the defensive and/or adaptive part that depressed affect plays in keeping repressed aggression at bay (43). This may accompany more immediate therapeutic change during dynamic therapy, i.e., cathartic relief through confession of unexpressed feelings. However, the latter method has been criticized as overused in psychodynamic practice, a carryover of the theoretical equation of aggression and depression in earlier psychodynamic thinking (43). It also is anachronistic in that it predates the significant transition in analytic thinking from catharsis to insight as the crucial agent of change (35).

As old modes of behavior are interpreted and clarified, the patient better understands his self-defeating way of attempting to gain self-esteem, excessive expectations of nurturance, need for proof of love and praise by idealized others, disappointment in parental affection, and consequent sense of failure and fears of abandonment. As insights are incorporated into his life over time in and outside of therapy, they can gradually form a permanent foundation for preventing future depressive episodes. That is, with some resolution of conflictual feelings, the patient can search for more gratifying, realistic ways to achieve a sense of worth.

The psychodynamic approach—whether long- or short-term—thus aims to modify the structural substrate of the depressive disorder, not merely its immediate manifestations. Resolving intrapsychic conflict related to significant others in the patient's present and past effects a reorganization of ego and superego structures, not simply symptomatic relief (29). More specifically, the psychodynamic model may be regarded as having several successive goals for the depressive patient, which are in part contingent on length of treatment: 1) to provide symptom relief through cathartic expression of suppressed aggressive feelings, 2) to lower superego demands and perfectionistic standards so as to reduce feelings of guilt and inadequacy, thus allowing self-esteem to be raised, 3) to make clear how current narcissistic wishes for love and excessive expectations in significant relationships are unrealistic and misdirected, i.e., how they are unwittingly repeated in actions toward others and aggressively turned against the self, and 4) to uncover and recreate the earlier conflicts from which the current disorder derives (3, 29, 43).

## COGNITIVE APPROACH

### *Concepts of Pathology and Etiology*

The major historical roots of the cognitive approach to depression can be traced from first-century Greek Stoicism and ancient Eastern religion to two modern influences of the twentieth century: phenomenology and its once ardent adversary, behaviorism. The early Stoics believed that a wise man is free from passion, unmoved by grief or joy, and submissive to natural law, and they were among the first to contend that the control of intense feelings could be accomplished by altering one's ideas. Epictetus (55–135 A.D.), a proponent of this stance in Rome, forecast the cognitive concept of pathology in his succinct statement "Men are disturbed not by things but by the views which they take of them."

Although Freud (45) did initially present the thesis that affect and symptoms are founded in unconscious ideas, i.e., mental representations of physiologic excitations, Adler's school of individual psychology was instrumental in applying the view that repressed experiences, such as infantile sexual traumas, are less significant than the patient's own self-determined, conscious perceptions of these events; Adler named this personal representation of external reality the "phenomenal field" (47). The behaviorist tradition was superimposed on these phenomenologic premises, with its theoretic emphasis on environmental learning and its technical use of conscious control in the modification of behavior. A crucial transition, however, was the shift from classical conditioning to an information processing behavioral model, i.e., from an emphasis on actions to stress on cognitions (48). On the American front, Kelly's psychology of personal constructs (49) was a specific therapeutic approach designed to alter patients' conscious experience; his fixed role technique, for example, has the patient assume a role incongruent with his typical assumptions about himself and his world and, by so doing, confront the erroneous personal constructs that are damaging his life. In a comparable vein, Ellis's rational-emotive therapy (50) directly attacks irrational false beliefs; his ABC theory involves intervention of a person's beliefs (B) between an activating environmental event (A) and its emotional consequences (C).

While several theorists have since contributed to the cognitive-behavioral framework and its application to psychopathology, the culminating developments in the cognitive approach to depressive disorders occurred over a decade and a half (1963–1979) of systematic clinical observations and experimental testing by Beck, Rush, and their associates (4). Initial impetus for the application of their cognitive thesis about depression came from experimental investigations of the dreams of depressive patients: instead of yielding Freudian unconscious, wish-fulfilling, masochistic content full of repressed rage and guilt, the dreams revealed repetitive themes of rejection, disappointment, and injury that matched the patients' conscious views when they were awake. Moreover, such self-deprecating cognitive constructs about individual patients proved objectively false, i.e., independent of empirical evidence (51).

### *Current Directions*

Currently, the major guidelines to the use and validation of a cognitive model in the treatment of depression are the work of Beck and associates (4). In essence, Beck's cognitive theory of depression posits that negatively distorted thinking patterns (ideas and images) are the basis for depressed behavior and symptoms; in short, dysphoria is a disturbance of cognition, not mood. Beck and associates expressly pointed out that such a theory addresses not ultimate etiology (such as hereditary disposition or faulty learning) but, rather, how maladaptations in cognitive structure, i.e., defective information processing mechanisms, predispose the individual to depressive disorder (4).

It is now theorized that there are three central maladaptive elements of depressive psychopathology: 1) a cognitive triad of recurrent negative views, which directly shape how the person sees himself, the world, and the future, 2) implicit irrational schemata based on the past by which the individual personally gathers, translates, and labels experiences, and 3) logical errors that pervade the assessment of one's self and life events. The cognitive triad comprises self-concept distortions (e.g., pronounced evaluation of oneself as deficient, defective, and/or undeserving), an overestimation of the environment (e.g., as unduly demanding, depriving, and/or rejecting), and a pessimistic view of the future (e.g., as without promise, value, or meaning). The other two characteristics considered essential to the maintenance of depressive symptoms, silent assumptions and logical errors, accompany this fundamental triad and compound its dysfunctional effects. Silent assumptions are rigidly held, covert, nonverbal axioms (usually misconceptions about love, approval, achievement, and the like) from which depressive persons draw their negative conclusions (e.g., If I don't win X's love, I am unworthy; If disappointing event X occurs in my presence, it's my fault; If goal X is denied me once, it will never be mine). Integral to these assumptions are errors in logic, which lead to irrational and exaggerated deductions. These faulty reasoning processes include selective attention, i.e., perceiving and focusing on certain dark features of an event while overlooking others; overgeneralization, i.e., using a solitary incident as the basis of sweeping conclusions about one's self and the future; and personalization, i.e., considering oneself the central or causative agent in events for which one is not realistically responsible. Such cognitive experiences are regarded as idiosyncratic to depression in both process as well as content, in that they are invariably automatic, persistent, and devoted to the overriding theme of loss (52).

### *Major Tools and Practices*

Cognitive therapy is standardized and brief (15–20 interviews) and is characterized by highly specific learning experiences; each session consists of a review of reactions to and results of the previous session, planning, specific tasks, and assignment of homework (4). The major modus operandi of the cognitive approach is logical analysis (12), application of the basic principles of logic and experimental investigation (i.e., data collection, inductive questioning, hypothesis formation, prediction, postulation of alternative explanations, and validation in reality) to the automatic tenets by which the depressed patient perceives, organizes, and responds to the world around him. Each persistent negative construct that accompanies depressed affect (e.g., I am a bad person; Nobody likes me; I am going to fail) is identified, its frequency and circumstances are noted, and it is posed as a specific testable hypothesis to which rules of reason are applied and for which evidence is gathered from everyday events (4).

To initially orient and involve the patient, he is assigned concrete reading material on coping with depression (53) and written self-reports (a weekly activity schedule to chart tangible behaviors, a mastery and pleasure schedule to rank degree of gratification and accomplishment). Both counteract initial passivity and demonstrate a direct way for depressed individuals to begin to gain greater control over their lives, i.e., by planning more productive activities.

Thereafter, special cognitive strategies help the patient to 1) detect, record, and review depressogenic beliefs identified in the patient's daily record of dysfunctional thoughts and deduce distorted assumptions, 2) recognize the relationship between irrational cognitions and self-defeating experiences, using concrete examples from recent events, 3) locate recurrent themes, such as fear of failure and the need to be perfect, through explicit assistance in categorization, 4) correct these perceptions by conducting mini-projects of progressive difficulty ("graded task assignments") (M.R. Goldfried, personal communication, 1979), 5) find explanations of events that are more rational and positive by using reattribution techniques, which challenge the depressed patient's dominant axiom of total responsibility for adverse occurrences, and ultimately, 6) progressively develop more adaptive and gratifying thinking patterns through repeated logical analysis, collection of evidence, and trial application in real-life situations. In addition, assertiveness training, role playing, and cognitive rehearsal (modeling and practice through dramatization or imagination) enable the patient to actively master specific scenarios, which serve as models for real-life achievement.

### *Therapeutic Relationship and Therapist Role*

The term "collaborative empiricism" has been coined to characterize the major therapeutic relationship in cognitive therapy, in which "the therapist is continually active and deliberately interacting with the patient" (4, p. 6). The two participants have been further depicted as an investigative team; the content of each depressed thought is posed as a hypothesis to be tested by two scientists, who collect all the evidence in order to support or refute that hypothesis (12).

To foster a rational collaboration, the cognitive therapist gives special attention to openly preparing the patient for what will transpire each step of the way, with explicit instruction and supplementary reading. Since the patient's active participation may be at least initially compromised by the depressive symptoms (e.g., lack of energy or motivation, difficulties in concentration), the therapist also engages the patient by gaining his explicit agreement to the treatment plan and thereafter involves him in specific tasks. This engagement includes joint selection of a target problem and continual feedback throughout the treatment (e.g., constant inquiry as to the patient's reactions, written appraisals of each session for postsession review) (12).

Under the collaborative empiricism model, the major role of the therapist is primarily educative (4, p. 404)—to instruct and advise the patient in rational thinking and to provide active guidance during systematic reality testing, which is considered intrinsic to the cognitive approach. The therapist actively points out automatic thoughts, helps to identify cognitions from the patient's report of recent experiences, reviews patient records, assigns homework, and provides concrete feedback. Often part of this tutorial approach is a direct problem-solving question-and-answer format, with which the therapist and patient can jointly explore the patient's cognitions. Although the therapist is thus a "teacher/shaper," a descriptor that characterizes the overall behavioral model of psychotherapy (44), with depressed patients he especially avoids authoritarian acts, such as interrogation or manipulation, which can exacerbate feelings of inadequacy and powerlessness. In Young and Beck's terms (54), it is a process of discovery, not persuasion.

In fact, because it is considered crucial to minimize negative responses, to which depressed persons are particularly prone, the therapist attempts to maintain a positive alliance at all times. By implicitly employing positive transference elements, he thus diffuses or avoids the development of irrational transference, which can lead to disappointment or dysphoric reactions. Such responses are not always avoidable, and they are dealt with immediately through conscious mutual examination: the patient writes down all the characteristics attributed to the therapist, and the patient and therapist jointly scrutinize their content logically, as with any other cognitive distortion.

### *Major Goals and Mechanisms of Change*

Whereas in typical behavior modification alterations in overt behavior are viewed as an end in themselves, with the cognitive approach they are considered a means to cognitive change (4, p. 4). The goals of this approach have been succinctly stated by its originators: "to teach the patient the following operations: (1) to monitor his negative, automatic thoughts (cognitions); (2) to recognize the connections between cognition, affect, and behavior; (3) to examine the evidence for and against his distorted automatic thought; (4) to substitute more reality-oriented interpretations for these biased cognitions; and (5) to learn to identify and alter the dysfunctional beliefs which predispose him to distort his experiences" (4, p. 4).

The major cognitive aims or processes of change have three successive components: recognition of faulty thinking through self-monitoring, modification of thinking patterns through systematic evaluation and empirical testing of the validity of automatic thoughts and silent assumptions, and self-mastery by means of homework and everyday practice on one's own (8).

The initial phase of treatment, which aims at symptom reduction, emphasizes the recognition of self-destructive thoughts, whereas the subsequent phases, which aim at prophylaxis, concentrate on the modification of specific erroneous assumptions within and outside the treatment sessions. To isolate, control, and change illogical thinking—the cognitive concept of cure—treatment is organized to elicit and subject to rational examination the actual mental contents of conscious depressive ideation (current automatic thoughts, silent assumptions, attitudes, values, daydreams) and to trace their impact on dysphoric feelings and behaviors in current concrete situations. Its ultimate purpose is self-control and self-mastery—the patient explicitly rehearses and trains himself to recognize and restructure his own faulty cognitions so he can cope better in the future.

## INTERPERSONAL APPROACH

### *Concepts of Pathology and Etiology*

Although the interpersonal approach to depressive disorder subscribes to a pluralistic point of view (i.e., the belief that no single cause in itself can explain depression) (5, p. 38), it is nonetheless founded on the hypothesis that the crucial factor in depression is the social network or interpersonal milieu of the patient. More specifically, it holds that disturbed social roles and unsatisfactory interpersonal relationships (especially the absence or loss of significant others) in childhood and/or adulthood can be antecedents to and/or consequences of depressive disorders and can play a part in both causal and risk factors (3).

The beginnings of the interpersonal model of pathology and treatment were largely the theoretical contributions of the Swiss-born psychiatrist Adolf Meyer and his American associate at Johns Hopkins, Harry Stack Sullivan. Meyer's innovative psychobiology (55) was pivotal in its application of the Darwinian concept of biological adaptation (56) to the understanding of psychiatric disorders; such a disorder was seen in terms of social adaptation, as the consequence of the individual's attempts to adapt to his surroundings. Early developmental experiences, especially family and environmental influences, were construed as the critical factors in the person's subsequent responses to the events around him. Sullivan (57) went further in concretizing these ideas; the Washington school of psychiatry represented an interpersonal approach that applied the cultural context of personality development to the arena of clinical psychiatry, drawing from anthropology, sociology, and social psychology. It was distinctive in viewing psychiatry as the scientific study of interpersonal relations (which challenged the basic Freudian concept of an instinctual sexual and intrapsychic basis for psychopathology). Although many of the founders and proponents of this approach (e.g. Frieda Fromm-Reichmann, Karen Horney, Erich Fromm, and

Sullivan himself) had originally been trained in psychoanalysis and did not necessarily reject such fundamental analytic constructs as the unconscious or the major role of childhood experiences, they placed much greater emphasis on social, cultural, and familial factors than on biological or dynamic internal forces.

### *Current Directions*

The Washington school laid the groundwork for the interpersonal approach to depression by shifting away from social psychiatric approaches that focused on large units of culture or society and on macroscopic environmental events, such as urbanization or the influence of social class. Rather, the unit of observation became the "primary social group, the immediate face-to-face involvement of the patient with one or more significant others" (5, p. 47). More specifically, it focuses on the individual's social circle, the most intimate family and love relationships, friendship, work, and community impact. The current interpersonal approach also stems from an assortment of research investigations with important implications for the study of depression: ethologic and experimental research in animal behavior, developmental studies of childhood, epidemiological surveys, and clinical investigations of adult psychopathology. These include the series of studies of mother-child and other attachment bonds (58–60), research on the relation of external life events to stress (61, 62), community surveys regarding the role of intimacy (63), and with the most direct implications, clinical explorations of the social relations of depressed adult patients (64).

The empirical findings from these studies highlight some of the basic concepts associated with this model: 1) the developmental importance of attachment or affectional bonds in depression—that is, the vulnerability of individuals to problematic interpersonal relations and psychiatric disorders if solid maternal bonds are not established early in life (58, 65)—and the relation of weak social bonds to depression (66, 67), 2) the notion of intimacy as protection against depression (63, 68, 69), 3) the relationship between recent stressful life events and the onset of depression (70, 71), and 4) the concordance between deterioration in all aspects of social functioning—e.g., poor communication, disruption of marriage or other major relationship—and the appearance of clinical depression (72, 73).

Childhood antecedents can be as specific as the actual absence or death of a parent early in life or, more likely, negative experiences related to the loss (5); childhood exposure to abuse, neglect, or family discord (74); and history of affective illness in the family (5). Similarly, adult antecedents include current social stressors (61), especially chronic marital discord, divorce, and separation (75).

In short, one's social bonds, their quality (how supportive) more than their quantity, are crucial to the individual's total adaptation and susceptibility to depression. The interpersonal approach thus places high priority, during illness and health, on the presence of gratifying intimate relationships with others and positive communication, primarily in marital and family relations but also in work, school, and peer relations (5). The most recent representation of this approach is Klerman et al.'s interpersonal therapy (5), which specifically recognizes four major interpersonal areas or problems that are commonly associated with major depression: 1) abnormal grief reaction, i.e., severe or unusual bereavement in response to the death of a significant other, 2) interpersonal role disputes, i.e., unreasonable, nonreciprocal expectations of or by significant others, especially disagreements about sex roles, 3) difficult role transitions—unsuccessful attempts to cope with developmental landmarks or with significant life events (positive or negative), such as getting married or divorced, having a child, graduating from school, changing careers, or retiring—and 4) interpersonal deficits, including inadequate social skills and history of social isolation or transient relationships.

### *Major Tools and Practices*

The interpersonal approach shares elements with both the psychodynamic and cognitive approaches and is, by the admission of its own proponents, not a new form of treatment (5). It emphasizes the solving of interpersonal problems and entails supportive and behavioral strategies as well as both directive and nondirective exploratory methods—information, guidance, reassurance, clarification, communication skills education, behavioral modification, and environmental management. Didactic educational techniques and environmental interventions are largely used in the initial efforts to ameliorate overt symptoms, whereas support, exploration, behavioral modification, and social skills training are subsequently applied to specific interpersonal issues.

The first phase of interpersonal treatment, which focuses on the immediate depressive symptoms, includes information gathering and assessment for both the therapist and patient. The therapist may use a structured interview (e.g., Schedule for Affective Disorders and Schizophrenia, Diagnostic Interview Schedule) that focuses on current life events and family history, especially events related to the depressive episode, and confirm these findings with explicit diagnostic queries to the patient.

The patient is also given direct information about depression as a clinical condition, often with the instruction to read recommended literature written in lay language (76). These efforts are all ultimately directed at legitimizing the sick role of the patient. This intentional, temporary therapeutic stance expresses the explicit alliance of interpersonal therapy with the medical model and is an important aspect of therapeutic improvement. (This does not, however, preclude the simultaneous minimization of dependency with suggestions that the patient engage in work and social activities whenever possible.) During the first phase

**TABLE 1. Major Features of Three Psychotherapeutic Approaches to Depression**

| Feature | Psychodynamic Approach | Cognitive Approach | Interpersonal Approach |
|---|---|---|---|
| Major theorists | Freud, Abraham, Jacobson, Kohut | Plato, Adler, Beck, Rush | Meyer, Sullivan, Klerman, Weissman |
| Concepts of pathology and etiology | Ego regression: damaged self-esteem and unresolved conflict due to childhood object loss and disappointment | Distorted thinking: dysphoria due to learned negative views of self, others, and the world | Impaired interpersonal relations: absent or unsatisfactory significant social bonds |
| Major goals and mechanisms of change | To promote personality change through understanding of past conflicts; to achieve insight into defenses, ego distortions, and superego defects; to provide a role model; to permit cathartic release of aggression | To provide symptomatic relief through alteration of target thoughts; to identify self-destructive cognitions; to modify specific erroneous assumptions; to promote self-control over thinking patterns | To provide symptomatic relief through solution of current interpersonal problems; to reduce stress involving family or work; to improve interpersonal communication skills |
| Primary techniques and practices | Expressive/empathic: fully or partially analyzing transference and resistance; confronting defenses; clarifying ego and superego distortions | Behavioral/cognitive: recording and monitoring cognitions; correcting distorted themes with logic and experimental testing; providing alternative thought content; homework | Communicative/environmental: clarifying and managing maladaptive relationships and learning new ones through communication and social skills training; providing information on illness |
| Therapist role/ therapeutic relationship | Interpreter/reflector: establishment and exploration of transference; therapeutic alliance for benign dependency and empathic understanding | Educator/shaper: positive relationship instead of transference; collaborative empiricism as basis for joint scientific (logical) task | Explorer/prescriber: positive relationship/transference without interpretation; active therapist role for influence and advocacy |
| Marital/family role | Full individual confidentiality; exclusion of significant others except in life-threatening situations | Use of spouse as objective reporter; couples therapy for disturbed cognitions sustained in marital relationship | Integral role of spouse in treatment; examination of spouse's role in patient's predisposition to depression and impact of illness on marriage |

the therapist also assesses current interpersonal relationships and the specific problem area to be addressed. The formation of a therapeutic contract is another goal of the first phase and provides the patient with an explicit treatment plan. This phase entails essentially didactic discussion, supportive exploration, and management of the patient's immediate interpersonal environment.

The middle phase, which is the crux of treatment, addresses the identified primary problem area. Each of the four hypothesized basic problems has its own therapeutic tasks and strategies in the here-and-now. For example, in dealing with abnormal grief reactions, a major technique is facilitation of the mourning process to allow expression and exploration of affects surrounding the loss, both positive and negative—sadness, guilt, and remorse, as well as good feelings, courage, and hope for new beginnings. This provides not only cathartic relief but a broader perspective, an alternative way of looking at the lost relationship. At the same time, the therapist is supportively offered as a temporary object who substitutes for the lost person until real replacements can be fostered through new involvements outside of therapy and the acquisition of additional social skills and interests.

In dealing with interpersonal role disputes, whether they involve marital, parental, employment, or peer networks, identification of the disagreement relating to the depression is the initial task and includes locating the predominant stage of the role dispute—complete dissolution, temporary impasse, or amenability to renegotiation (5). Here the patient is encouraged to examine maladaptive perceptions, faulty communications, and nonreciprocal expectations that are exacerbating the problem, as the therapist helps to clarify them and guide the patient into new ways of relating to others and alternative interpersonal behaviors. This often entails communication analysis and training in new communication skills.

In addressing a role transition, the therapist may have to deal with the patient's equation of significant life changes with loss; the patient's response to such developmental events or alterations is like a grief reaction. A major strategy, however, is to assist the patient in distinguishing such events from real losses and to guide him in abandoning the old roles and preparing for new interpersonal tasks. Here the emphasis is on a larger repertoire of social skills and on interpersonal mastery, which will improve the patient's adaptation to the demands of his current roles. The theme with such role transitions, as in abnormal grief, is the use of losses as opportunities for new possibilities and growth.

Interpersonal deficits generally involve lack of the experience and interpersonal skills required to initiate or sustain relationships. Although severe social isolation may represent a more serious disturbance, many of the interpersonal problems of depressive patients can be altered through clarification of the positive and negative aspects of relationships, social skills training, and other behavioral modification techniques. In each instance, a positive relationship with the therapist can

**TABLE 2. Advantages and Limitations of Three Psychotherapeutic Approaches to Depression**

| Feature | Psychodynamic Approach | Cognitive Approach | Interpersonal Approach |
|---|---|---|---|
| Theory | | | |
| Advantages | Individual depth approach encourages patient to look inward for solutions rather than depending on external sources | Cognitive/behavioral orientation is tangible and objective | Interpersonal orientation addresses broader (e.g., social, family) context, useful in focusing on man-woman relations |
| Limitations | Focus on intrapsychic phenomena may obscure other (e.g., interpersonal, environmental) factors; aggression=depression theory can be overgeneralized and lead to overreliance on catharsis | Cognitive/behavioral emphasis may neglect whole person, especially affective component; symptom-oriented perspective overlooks past history, complex problem areas, and hidden conflicts | Emphasis on four designated interpersonal problems can bias toward preconceived themes; interpersonal orientation may stress marital/family factors while underplaying intrapsychic forces |
| Goals | | | |
| Advantages | Enduring structural change transcends symptomatic relief; strengthened adaptive capacities can be useful beyond specific depressive pathology | Primary goal of symptom relief is expedient in itself and is first stage in changing cognitive style | Improvement of interpersonal relations is expedient in itself and may also result in relief of symptoms |
| Limitations | Personality alteration can be too ambitious and may be unnecessary or excessive for most depression diagnoses | Symptom reduction may be insufficient, superficial, or temporary; focus on current problems can preclude enduring modification of personality or prophylactic function of treatment | Symptom relief may be fragile and temporary if it is highly dependent on external factors |
| Structure | | | |
| Advantages | Indefinite duration allows long-term or flexible goals[a] | Brief or fixed duration is cost-effective and can foster results in short period, may heighten expectation of rapid change and encourage optimism | Predetermined duration is cost-effective; approach reengages family and may have preventive effect |
| Limitations | Long-term or open-ended treatment is uneconomical and difficult to evaluate[a] | Short or predetermined duration may be insufficient or inflexible | Time limitation predetermines the extent of personal growth and independence |
| Therapist role | | | |
| Advantages | Neutral, accepting stance ensures nonjudgmental attitude and objectivity; receptive listening encourages transference formation and ensuing analytic process | Active therapist can directly intervene to interrupt depressive schemata and suggest alternatives to faulty thinking | Therapist position between activity and reactivity can reassure patient and provide supportive person for patient to relate to |
| Limitations | Transference regression can produce overidealization of therapist and underestimation of patient self-worth; therapist silence may be misconstrued as rejection, which can perpetuate depression and/or cause premature termination | Active suggestion and direction can undermine patient responsibility and self-esteem by imposing therapist point of view or values | Supportive interpersonal role may encourage dependency and rage at withdrawal of therapist |
| Techniques | | | |
| Advantages | Free association provides verbal catharsis; interpretations provide new understanding of depressogenic conflicts and historical events | Specific approach is directly tailored to depressed population and aims at particular target symptoms; identification of depressogenic assumptions and homework to test new thinking foster cognitive modification | Specific approach is directly tailored to depressed population and can address particular current interpersonal maladaptations |
| Limitations | No specific techniques developed; focus on past events and spontaneous associations may encourage repetitive litany of depressive complaints at the expense of present therapeutic tasks | Emphasis on specific cognitive schemata may bias toward certain preconceived themes; overt simplicity of techniques may lead to underestimation of technical skill required | Identification of specific interpersonal problem areas may be overly restrictive, yet techniques are relatively nonspecific; legitimation of patient sick role may encourage passivity |
| Research status | | | |
| Advantages | Longitudinal case study approach useful for detailed examination and follow-up of individual patients | Operational manual allows for replication of treatment and training and empirical establishment of efficacy | Same as for cognitive approach |
| Limitations | Idiographic approach or anecdotal case history is not amenable to controlled or comparative research | Research-oriented operationalized approach may become oversimplified formula for complex clinical phenomena | Same as for cognitive approach |

**TABLE 2 (continued)**

| Feature | Psychodynamic Approach | Cognitive Approach | Interpersonal Approach |
|---|---|---|---|
| Relation to other modalities | | | |
| Advantages | Integrity of transference is maintained through elimination of outside influences | Competition with pharmacotherapy encourages research on relative efficacy, especially instances when cognitive therapy alone is most effective | Approach designed to be used alone or with drugs; it is especially amenable to combination with marital therapy (manual is being developed for using conjoint marriage therapy as adjunct to individual treatment) |
| Limitations | Need for neutrality may limit use of other helpful treatment approaches (e.g., family therapy, drug treatment) | Competition with pharmacotherapy fosters polarization of approaches and partisan resistance to integration with drug treatment | Amenability to additive or eclectic modalities requires integrative theoretical model, clinical expertise in more than one modality, and/or ability to collaborate with other disciplines, which may lead to role diffusion and insufficient knowledge or training |
| Patient population | | | |
| Advantages | Special patient requisites (e.g., verbal orientation, psychological-mindedness) ensure maximal insight | Logical thinking ensures maximal potential to deal with and change depressogenic assumptions and thought patterns | Orientation toward interpersonal relations, especially marital interaction, can address gender issues in marriage, especially important given high prevalence of women among depressed patients |
| Limitations | Special patient requisites may limit usefulness to verbal, psychological-minded population | Cognitively impaired population may not benefit; sophisticated, introspective patients may find approach too simple-minded or superficial | Interpersonal orientation may overemphasize marriage; primarily female population may bias toward women; conjoint focus may bias against unmarried population |

[a] Advantages/limitations of short-term psychodynamic therapy are similar to those for the cognitive and interpersonal approaches.

serve as a model and provide practice for future relationships during the ongoing negotiation of problematic interpersonal scenarios during therapy.

### *Therapeutic Relationship and Therapist Role*

According to its originators, the therapeutic relationship in interpersonal therapy is explicitly "not . . . the primary focus of treatment" (5, p. 149). Nonetheless, the role of the therapist and use of the therapeutic relationship have been delineated according to the following major guidelines.

1. The therapist is an advocate of the patient, not neutral. The therapist's essential role is as a benign and helpful ally who is basically supportive while offering direct advice and reassurance.
2. The interpersonal therapist takes a deliberately directive stance, but in actual practice it represents a moderate position between highly active and highly reactive; the therapeutic role is both prescriptive and exploratory.
3. The therapeutic relationship is not interpreted as transference; it is predominantly realistic, directed at problem solving to keep the patient from becoming too dependent or regressed. The major exception to this stance, however, is when the patient's response to the therapist is interfering with treatment, whereupon explicit attention is given to the relationship.

Aside from these general axioms, the therapeutic relationship can also be used as a specific means of addressing each of the major problem areas in depression. In the case of role disputes, direct feedback on how the depressed patient is perceived by others can be provided through similar interaction with the therapist and can then become a basis for communication and decision analysis. For a patient experiencing grief or loss, reactions to the therapist may mirror either the patient's relationship with the lost person or the manner in which he responds to other situations of interpersonal abandonment. In the case of social deficits, the relationship with the therapist becomes a model for the development of relationship skills.

### *Major Goals and Mechanisms of Change*

The fundamental goals of the interpersonal approach relate to the need to maintain good interpersonal relations and social adaptability; they include reconstruction of present maladaptive relationships and, where possible, restoration of past losses. This means both coping with immediate stressful interactions and forming better or new relationships by developing problem-solving strategies and mastery in social skills. The therapist may also facilitate the mourning process for a patient who is actually or psychologically bereaved, then encourage him to find substitutes for the lost object and to use the loss as a means of growth. A more immediate goal, however, is the direct alleviation of depressive vegetative signs and symptoms, which acts as a preface to (and to some extent is independent of) the special interpersonal problem areas that are the heart of treatment.

Other interpersonal therapy tasks are minimizing dependency by helping the patient to better negotiate current relationships (including his relationship to the therapist) and maintain important social roles vis-à-vis work, family, and peers, thereby improving self-esteem. While the interpersonal approach reduces dependency, an early educational aim is to facilitate the patient's acceptance of depression as a sanctioned and real medical illness (5). In sum, according to the originators of interpersonal therapy, the goals of interpersonal therapy fall into two major categories—symptom formation and social and interpersonal relations (5).

Table 1 is a comparison of the major features of the three psychotherapeutic approaches to depression.

## ADVANTAGES AND LIMITATIONS OF THE THREE APPROACHES

Both advantages and disadvantages of each of the three psychotherapeutic approaches to depression are presented in table 2.

Often the greatest contrast occurs when comparing the psychodynamic approach with the other two. This is in part because of the former's historical role in the development of the psychotherapies. Many forms of psychotherapy developed since Freud's time have addressed presumed failings of the psychoanalytic model; they are thus deliberate theoretical and/or technical departures from it, at least overtly (44). Placed in chronological perspective, for example, the analytic approach has the disadvantage of having originated as a general treatment of neuroses (chiefly characterized by anxiety) and was never designed for depressive disorders (33), whereas cognitive therapy and interpersonal therapy were specifically devised for depression (4, 5). In addition, although the analyst is an intentionally neutral and objective observer, the psychodynamic approach—which is based on the individual case study method, disguised (unconscious) data, and often open-ended time frame—has traditionally been the least amenable to standardization and research. This has limited attempts to replicate treatment and training and to empirically establish efficacy (9, 77, 78). Moreover, its ambitious aim of modifying personality structure, sometimes within a relatively short period, may seem difficult in this day and age, especially with increased public pressure to demonstrate discernible effects in a short time.

With regard to both theory and techniques, the special problems of a psychodynamic approach to depression usually fall into three major categories: 1) overuse of catharsis, 2) pitfalls of a regressive transference and negative response to therapist silence, and 3) undue priority given to individual dynamics and the dyadic relationship as a closed system. Mendelson (43) has observed that equating depression with unconscious aggression in dynamic theory may foster overuse of the cathartic model. This formula may be fallacious both conceptually and clinically: theoretically, depression may be more of an ego than superego problem (a defect in self development, not simply an excess of aggressive cathexes), and technically it may be a mistake to focus on hostile feelings, especially early in treatment, since self-esteem must often be raised before anger can be usefully expressed, not the reverse.

With regard to transference, it has frequently been observed that the clinical manifestations of depression include persistent requests for magical relief and manipulative attempts by the patient to gain nurturance. Jacobson (29) has described the perils of allowing development of an unrealistic idealization of the therapist, to which patients in psychodynamic therapy are particularly prone. Although some degree of illusion is essential to the transferential process, and may even be therapeutic in the treatment of depressed borderline patients, it may unwittingly foster the very dynamics it tries to cure, i.e., excessive demands for love and gratification from an external source, if it is not worked through. Another danger of the analytic stance with depressed patients, who already have poor self-esteem, is the likelihood that therapist silence will be construed as rejection, leading to more depression and/or flight (11). In fact, Bemporad (42) recommended that the psychodynamic therapist not become a major focus of the patient's life and that, to break the monotonous litany of depressive complaints, the therapist needs to actively introduce new content, not remain reflective.

Finally, the traditional focus on the individual patient to the exclusion of outside contact may especially compromise treatment of depression, insofar as such patients are often unable to relinquish a premorbid relationship (e.g., with a spouse) that may predispose them to the illness. In such cases, it would be advisable to see the partners together or to arrange for family intervention (42). Forrest (79) stated that because of the reciprocal reinforcement of depression in marriage, it may be essential to see both parties, although such practices have traditionally been avoided in psychodynamic circles.

The total picture is balanced by the advantages of structural and technical aspects and the goals of the psychodynamic approach. For example, its introspective strategy encourages an inward search for solutions as an adaptive alternative to pathological reliance on external sources of esteem. The often open-ended orientation allows for a flexible response to patient needs and greater attention to the long-range future. Goals that transcend symptomatic relief can be useful beyond specific targeted problems, i.e., to strengthen general ego capacities and increase the prospects of permanent structural change. In addition, some of the flaws traditionally associated with psychodynamic therapy are being corrected by significant revisions in therapy format, strategy, and research (e.g., brief duration, combination of expressive and supportive techniques, development of standardized manuals) (6, 7).

A major advantage of cognitive therapy is that the therapist can directly intervene; it is used to interrupt thought patterns and actively help patients learn and practice logical alternatives. A fundamental asset of interpersonal therapy is that it addresses the broader social context of depressive risk and engages the family in treatment. Although both of these approaches are tailor-made for depression and offer obvious practical benefits, they are not without corresponding limitations. Highly focused aims may be too restricted, superficial, or temporary; emphasis on current problem areas or recent stresses can camouflage significant long-standing conflicts that need attention; a very directive approach may preempt patient initiative or discourage introspection; and a fixed-length or brief therapy can prematurely close off deeply concealed issues that take longer to emerge, allow less time for correcting diagnostic errors or overcoming resistances, or can even counteract treatment gains with a patient's disappointment about not achieving a more lasting cure. Moreover, the research need to operationalize treatment may foster reductionistic formulae that omit complex clinical phenomena or, more important, preclude the very nuances of individual technique and relationship that are crucial to personalized patient care.

Beyond the respective advantages and limitations of these particular approaches, all psychotherapies for depression may suffer from some of the same constraints, e.g., dedication to a particular point of view and resulting bias toward certain preferred themes or content areas. Examples are childhood conflicts, disappointment in parents, excessive guilt, and unexpressed rage (psychodynamic); marital disputes, environmental stresses, and gender or role problems (interpersonal); and preconceptions about self and future and illogical expectations of others (cognitive). The psychodynamic model may overemphasize unconscious processes and the primacy of affect (80), while cognitive therapy may overplay the role of thinking, and the interpersonal model may forgo the internal mechanisms of the disturbance for the socioenvironmental context in which it occurs.

## CONCLUSIONS

The first major U.S. public health prevention program for a specific group of mental disorders—the NIMH Depression Awareness, Recognition, and Treatment Program—suggests that from 80% to 90% of persons with major depressive disorder can be treated successfully (81). This multi-institutional project is using the newly standardized cognitive and interpersonal therapies and in the near future will begin clinical trials with short-term dynamic psychotherapy. These efforts should include determination of for whom and when these treatment modalities are appropriate and whether they are most effective together or separately. Preliminary trials with imipramine for unipolar depression also suggest the need to specify the principles for combining the psychotherapies with other significant treatment modalities for depression, such as pharmacotherapy.

The systematic comparison of the three major psychotherapeutic approaches to depression today—cognitive, interpersonal, and dynamic—reveals that, as in the larger field of psychiatry, each school or treatment modality appears to be different from the others (at least overtly) in terms of its theoretical orientation, major goals, mechanisms of change, and techniques. At the same time, delineating these dimensions and the advantages and limitations of each approach sets the stage for revealing both the distinct and complementary features of the different approaches—what a particular modality offers to different types of patients and how one or more modalities have positive effects on all patients. Ultimately, this may pave the way for treating individual depressed patients in a highly selective fashion, drawing from the therapeutic elements of all available approaches and using them together and separately.

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# The Evolution of Systems of Mental Health Care: The Arizona Experience

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*Reform in a system of mental health services is the result of a variety of forces that operate synergistically to bring about observed events. This evolutionary process is most likely to yield substantial results through multiple interventions over time rather than a single attempt at reform. A process of change in the mental health service system in Arizona has been evolving in response to the interaction of several key variables: a social movement dedicated to reform, a planned design for change, and the use of litigation. The author reviews each of these factors and assesses the overall process of change within the state.*

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What are the necessary conditions for effecting widespread reform in a mental health service system? Modifying the system of care is a process of such exquisite complexity that, often, when it occurs, we do not seem to understand what made it happen. We typically experience great difficulty both in identifying the precise variables that led to the change and in explaining the ways in which those variables interacted.

It is not surprising, therefore, that efforts to introduce reform often fall short of their intended goals. Lacking an understanding of the complexity of the process of change, we are apt to view the most obvious, although not necessarily the most relevant, variables as the effective agents. Accordingly, we might attempt to duplicate a "model program" in the belief that the demonstration of a successful intervention in one community will beget the process of change in another community. Or, noting the personal dimension of social change, we might attempt to recruit a charismatic leader. Or we might increase and redirect the allocation of funds in the expectation that increased resources will generate more responsive systems of care.

In this paper I will argue that, although all of these conditions may play some part in the process of change, none is, by itself, sufficient to generate dependable and lasting reform. Relying on any one of these solutions or others like them reflects an oversimplified view of the problem at hand. What is needed is a more global understanding of the multivariate nature of social reform, since such change does not occur as the result of the manipulation of a single variable. Furthermore, progress only rarely occurs from a single attempt at reform; a succession of several strategies designed to bring about change over time is usually required.

It is my contention that the process of reforming a mental health service system depends on the simultaneous manipulation of several variables. The conditions involved, however, will vary from place to place and are dependent on local circumstances. To illustrate my major thesis, I draw on the history of a recent reform effort that culminated in the "Arizona experiment" (1, 2), a unique plan to change treatment conditions and to improve access to services for the chronically mentally ill residents of Arizona. The Arizona experiment may be understood as a series of events within the state that occurred in response to a coordinated and directed plan. This social movement was set in motion to achieve a specific goal: a better system of care for the seriously mentally ill in the state.

Today's mental health service system in Arizona may thus be viewed as a cross-sectional slice in a longitudinal series of events. Many different variables interacted and generated the milieu within which reform was able to occur. Among these variables, there was first the creation and development of a social movement—a collective incentive of a grass-roots nature—defining and guiding the reform. Second, there was a detailed, officially approved plan outlining the mechanisms for proposed change. Third, there was litigation that brought visibility, consensual validation, and strength to the social movement.

## THE SOCIAL MOVEMENT

Collective behavior directed toward changing existing conditions can occur only when certain precondi-

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tions have been met. Smelser (3) enumerated six such preconditions: 1) a preexisting pattern of social organization conducive to the development of collective enterprise, 2) the presence of strain in the form of a difficult and intolerable situation whose eradication would bring relief to a substantial portion of the community, 3) a shared and generalized belief that provides the rationale for change, 4) precipitating or triggering events, 5) mobilization of agents (i.e., the formation of a group with a common identity and common understanding of the problem to propel the change), and 6) the presence of social control mechanisms to channel, hinder, or reinforce the collective behavior. I will discuss each of these preconditions with particular reference to the Arizona experience.

## *Preexisting Pattern of Social Organization*

During the 1970s, the efforts of several leaders in mental health planning led to the creation of what has since been called a "unified system of care" in the greater Tucson area (4).

Like any service initiative, however, Tucson's unified mental health service system was characterized by peaks and valleys, and the promise of the 1970s largely failed to carry over into the 1980s. The system was plagued by the same shortcomings of deinstitutionalization efforts reported by others (5). It also appears that when the leaders of the Tucson system were no longer available, the inherent problems in the service system began to multiply. Not even the local version of the community support program, a federally inspired initiative designed to target the most severely disabled chronically mentally ill individuals for care (6, 7), maintained the momentum. In the Tucson area, and even more markedly in the rest of the state, where progressive planning had never truly taken root, the combined effects of changing leadership, poorly processed deinstitutionalization plans, and abysmally low levels of funding led to a highly fragmented and ineffective system of care in which severely disabled chronically mentally ill patients appeared to have no established niche.

The void left by the departing leadership was quickly, even if not effectively, filled by those who held control over different parts of the system of care. The state's Division of Behavioral Health was unable to exercise enough authority and expertise to prevent the creation of fiefdoms and a merciless battle for turf. This unchecked process gave rise to four major factions in Tucson. The turf battles ended in a stalemate, since no one was able to develop sufficient power and lead a cohesive approach to the care of the mentally ill. State agencies, not-for-profit mental health centers, and counties engaged in a tough battle for control and survival and were caught in a gridlock.

Beginning in the late 1970s, a number of relatives of mentally ill persons, together with some mental health professionals and other concerned citizens, began to express dissatisfaction with the deficiencies and discriminatory practices characterizing the system of care. Given the lack of leadership at the state level and the inability of providers to form effective coalitions, I formulated a plan to coordinate the emerging dissatisfied factions into a collective movement that would, in turn, advocate a reform of the system of care. Deciding to forgo the potential benefits to be derived from mutual support among providers, I opted for a more polarized approach that clearly, even if at times simplistically and somewhat unfairly, identified the roots of the fragmentation and ineffectiveness. The County Board of Supervisors, to whom I answer, was sensitive to the existing problems and supportive of proposed solutions. The fragmentation and ineffectiveness were identified publicly through press reports to bring about maximum impact in the community.

Demonstration projects were used to underscore the effectiveness and feasibility of the proposed remedies. Aggressive outreach to severely disabled patients, including crisis intervention and long-term care, was implemented locally by the county system with great visibility and support. Furthermore, substantial cost savings were realized by effectively eliminating the county's use of private hospitals. All hospitalizations were limited to the county hospital. A community-based system of care was implemented to create home-bound alternatives to hospital care. This substantial cost reduction further strengthened the validity of the model proposed on behalf of the county and gave credence to the charge that the traditional system of care was unwilling to address its pervasive fragmentation and inefficiency.

At the same time, families of severely mentally ill patients were becoming more dissatisfied and impatient with the system of care. They formed the first chapter in Arizona of the National Alliance for the Mentally Ill (8). These families, along with the County Board of Supervisors, became the fundamental components of the emerging social movement. The media were eager to assist and began a continuous and repetitive campaign to educate the public on the issue. Special features on visible and successful programs and editorials denouncing abysmal conditions and demanding a solution appeared frequently.

Relations with the news media posed particular problems that required certain skills. Calls and inquiries had to be answered promptly. "No comment" was not an acceptable answer. Manipulation of the media was avoided by a frank, jargon-free, and unhurried exposition of the problems and the proposed solutions.

## *Presence of Strain*

The stage had been set for the supporters of reform to give a unified and therefore a stronger voice to their concerns. Early in the history of their coalescence they disseminated the difficulties that the chronically mentally ill and their relatives were encountering as the result of an inadequate and fragmented system of care. They made it clear that this inadequate system affected the community. They made their case in simple, persuasive language that, with media support, could be easily understood by the public. Supporters documented the relationship between deficits in the service system and escalating rates of suicide, alcohol and drug consumption, and homelessness. The problems they publicized were uniformly couched in human terms—anecdotes and case presentations depicting patients and their families in real-life situations. The media and increasing numbers of enlightened public officials eagerly participated in providing a forum to convey this information.

The information did not hesitate to identify the culprits: an inappropriate, sluggish, and discriminatory system of care; neglect of the problem by the state's executive branch; and an unresponsive legislature that was responsible for the State of Arizona's position as the state to allocate the lowest per capita funding for mental health services (9). In response, the state's Division of Behavioral Health, as well as a variety of mental health service providers, suggested some tentative reforms. However, their attempts fell considerably short of redress, probably because of widespread resistance to change.

The repeated and well-targeted efforts to expose the system's shortcomings eventually sensitized the entire community to the presence of an intolerable problem. The existence of strain was emphatically established and widely publicized, and soon the proposed reforms were widely supported.

### *Shared and Generalized Belief*

Shared belief is essential to the organization and growth of a social movement, because only with consensus can there be a common explanation for the causes of strain and a rationale for common action. The conviction shared by the members of the collective movement that the state's mental health service system was deficient and excluded those patients most in need of care certainly fulfilled this precondition. However, consensus is difficult to maintain when a social movement results from a coalition of groups with divergent views and goals. A shared and generalized belief is, at best, tenuous and lasts only as long as the separate beliefs of the coalescing interests are not undermined or violated.

The State of Arizona was and, in fact, continues to be characterized by diverse beliefs about the needs and rights of mentally ill individuals. The exceptionally large and sparsely populated rural portions of the state have values concerning these issues that differ from those found in urban communities. Indeed, it is not uncommon for rural communities to mistrust what they think of as urban solutions for social problems (10).

Values concerning these issues may vary even from city to city. For example, in Phoenix, the state capital and largest city, the opinions expressed in the mass media and by elected officials, as well as by family advocacy groups, were quite different from those expressed in Tucson, the second largest city. As the social movement progressed, each of these communities and their elected representatives seemed to be pursuing different goals.

Most importantly, the family advocacy movement, the most powerful and visible representative of the reform movement, was profoundly divided as the collective action began to take form. Local chapters of the National Alliance for the Mentally Ill had fundamental differences in their conceptualizations of patients' needs and what might constitute a proper system of care.

The differences in philosophy between the Phoenix and Tucson chapters of the family advocacy movement were played out in a rift. In Tucson, families and mental health professionals generally shared a belief in the superiority of community-based care for chronically mentally ill patients. They were apt to attribute system difficulties not to deinstitutionalization per se but to a flawed process of creating alternatives to institutional care. In Phoenix, however, opinions on this issue were split, and two family groups were formed. The predominant group coalesced around the conviction that state and county mental hospitals constituted the only viable answer to overcoming neglect of the chronically mentally ill. The other group shared with the Tucson chapter a belief in the superiority of community-based care, albeit to a lesser degree. The family movement supporting institutional care based its conclusion on the devastating failure of the community-based system to prevent neglect and catastrophic outcomes. The presence of a traditional and poorly funded community-based system of care without leadership to aggressively address the problems of the most seriously ill patients probably accounts for this attitude. The deficiencies were particularly notable in the lack of assertive outreach by community-based programs to the most disabled patients. The problem was probably compounded by the location of the state hospital in the Phoenix area, a constant and readily available environment to protect the patients from total neglect and life-threatening exposure in the community.

Ultimately, this factionalism in the family groups would prove to be the Achilles' heel of the social movement: it would weaken the effectiveness and negatively affect the collective action.

### *Precipitating Events*

The difficulties experienced by the chronically mentally ill and those concerned with their welfare were widely exposed by articulate spokespersons. What was still needed was a series of circumstances that could directly trigger concerted action. In some social movements, such precipitants are abrupt and easily identified; however, in this case, the precipitating events seemed to build more slowly to a point where they gradually took on explosive potential.

Given the presence of large numbers of neglected chronically mentally ill patients in the community, it is not surprising that there were also high rates of suicides, visible homelessness, and increases in the consumption of drugs and alcohol; these events underscored the plight of the mentally ill. Whether society's response to these events was based on fear, shame, guilt, or some combination, their very visibility served to lend credibility to the collective enterprise.

### *Mobilization*

The mobilization of forces to attack and change the status quo is critical in addressing social problems. It is through mobilization that society is provided with new norms for unstable situations during a period of change.

Mobilization typically requires the presence of individuals with a common identity and a common understanding of the problem. It also typically requires the presence of a highly structured organization devoted specifically to the task of promoting change. In Arizona, reflecting a national trend, the stage for mobilization was set by local chapters of the National Alliance for the Mentally Ill. A highly motivated, articulate membership, many of whom possessed strong organizational skills gained in other areas of their lives, in combination with effective leadership, formed the basis for the required mobilization. Not reluctant to use help wherever they found it, these relatives of the mentally ill, together with their disabled family members and concerned representatives of the legal and mental health professions, were critical to the social movement's progress.

There were, however, some weak links that reduced the overall effectiveness of the advocacy and lobbying efforts of the Arizona chapters of the National Alliance for the Mentally Ill. One of these, as noted, resulted from intense divisions of opinion concerning the preferred locus of care for the mentally ill. A second weak link resulted from the role conflicts that members of these organizations frequently and almost inevitably endured. With only a few exceptions, it was extremely difficult for these family members, most of whom were middle-class, to maintain a strong and consistently militant presence as advocates for reform. Their social positions in the community tended to cast them in the role of well-integrated, low-key, "good" citizens who did not "make waves."

Some family members who lobbied the legislative and executive branches in their professional lives found it difficult to use their influence in the service of their personal lives. It must be noted that some notable exceptions occurred. There were individuals who clearly jeopardized their professional effectiveness to advance the cause of their family members.

The other element that weakened mobilization was the sheer fatigue experienced by those who had to deal with the consequences of a poorly funded and constructed system of care. They simply found it beyond their means to participate further in struggles. A certain apathy, which was difficult to explain and was more pervasive than the sum total of dissatisfaction and complaints would justify, further weakened the social movement. A fear of retaliation by the established and threatened system of care also played an important role in the hesitancy displayed by many families. This is the "social control" with which the established system of care can expect to keep a reformation movement at bay.

### *Social Control*

A collective action takes root in the context of certain rules, regulations, and positive and negative sanctions that facilitate or hinder the proposed reform. This is the structure in which the social movement has to accomplish its goals.

The collective action in Arizona had strong public backing when it began its advocacy of a new normative structure for the delivery of mental health services. The social movement articulated its position loudly and clearly. New rules were now to take effect: all mentally ill individuals, including the most severely disabled among them, were to be entitled to the best in services; no discrimination based on degree of disability would be countenanced. Moreover, entitlement of the most seriously ill to care was to supersede maintaining the status quo as a goal of the social system even if the state bureaucracy was forced to adjust its operations to accomplish this end. Facilities and their bureaucratic superstructures would have to change their practices at any costs, and financing of state care for the mentally ill would follow. Adequate funds would be made available to patients wherever they happened to be, whether in the community or in the state mental hospital. Finally, state-supported community mental health centers would change their practices to become more accessible to the chronically mentally ill and, better yet, would actively invite those patients in for care in an assertive manner.

Stirrings of responsiveness were now emanating from the executive and legislative branches of state government. Given the previous lack of concern, the changing attitudes of the government leaders served as additional powerful sanctions. However, social control may be a two-edged sword. The administrative and legal structure, with its corresponding requirements to effect reform, may require a process that will help the established system to channel, control, and ultimately resist change whenever it is perceived as too threatening.

In Arizona, the executive and legislative branches of government had previously used a variety of formal and informal means to prevent progress in mental health funding and service delivery. Even when the idea of reform as a timely necessity was finally accepted (1), several administrators continued to resist change. For example, some individual legislative staff members used their power to sway the opinions of legislators and to influence the direction of proposed statutory change. These actions created dissension within the government and even generated basic doubt as to the motives of the social movement. The ability of the dissenting public servants to sabotage the efforts of the social movement was considerable, since they wrote the statutes and, therefore, exerted control over the final product.

In the face of these circumstances, the proponents of reform were forced to negotiate not only with the legislators themselves but also with members of the legislative staff, and they had to become quite adept in political maneuvering.

The legislative branch was not alone in its effort to frustrate change. The executive branch, through the Division of Behavioral Health, also exerted considerable control through inaction and resistance. In addition, when legislation was finally proposed, a layer of middle management representing the state's not-for-profit mental health service providers retained a lobbyist to defeat the proposed reform.

It appears that the proposal of a new set of norms, regardless of how persuasive and organized the proponents of change may be, is by itself not sufficient for a social movement to gain the upper hand. In the Arizona experience, advocates confronted massive administrative resistance. Some public servants were unable to accept measures that, by implication, indicted them. Others were simply too threatened by changes that might disrupt their turf or eliminate their programs altogether. Many were persuaded that the system's failures should be attributed not to discrimination and fragmentation but to a simple lack of resources. They were supported in this contention by the extremely low rank among the states that Arizona held in per capita spending for the mentally ill (9). The attempts to change the rules of the game—i.e., to redefine the normative structure—thus resulted in a hardening of positions rather than in progress toward ending discriminatory practices.

More than likely, the suggested reforms proved to be too threatening to the bureaucratic structure. By failing to change the attitudes and beliefs of the public servants who represented and managed the bureaucracy, the collective action was able to claim only partial success. The legislative branch fell short of passing comprehensive reforms in the state system of care. However, in a spirit of compromise, it agreed to embark on a pilot study to test a radically different service delivery style (1). The social movement would have to accept partial success—a pilot project to be implemented in selected parts of the state: a tentative trial at reform that might eventually bolster the cause.

## PLANNED CHANGE

The second force that operated within the established mental health system was the planning and reform efforts initiated by the system itself. Despite the resistance of many public officials, it became imperative to enlist the efforts of concerned and knowledgeable professionals in the area of mental health service planning to prepare a structured and codified statement detailing the proposed reform. This was accomplished through the efforts of the state's Division of Behavioral Health, which had opposed the legislative bills introducing the pilot project. Once the statutes became law, the Division had no alternative but to develop a blueprint for the pilot project, complete with problem statements, population definitions, guidelines, and time lines for change.

There was little in the way of precedent to guide these efforts. The Division of Behavioral Health had in fact previously attempted to introduce several plans to improve the system of care. These plans were deficient in their failure to address the multivariate aspects of system changes identified by Davis and Salasin (11) as critical for the successful implementation of plans to reform systems of mental health care. Predictably, they resulted in partial, fragmented, and ultimately ineffective attempts at reform. The only truly successful previous plan for change in Arizona had taken place in the early 1970s in Tucson (4) and in northern Arizona.

In spite of these constraints, however, the Division of Behavioral Health did succeed in implementing the blueprint for system modification based on the pilot project. The cornerstones of that plan have been described elsewhere (1), and they include the following tenets: 1) that the system will protect, as much as possible, the needs of each individual patient and that the system will follow established principles of continuity of care (12), 2) that eligibility for access to the system of care will be based on a statutory definition of chronic mental illness emphasizing disability and duration rather than diagnosis or institutional history, 3) that patients will be under the care of clinical teams who will provide them with access to a full continuum of services and, as such, function as "gatekeepers," 4) that the treatment plans for each patient will involve a negotiation reflecting a real empowerment of patients and their families, and 5) that the teams will be funded on a prepaid, per capita basis.

## LITIGATION

The third interactive variable leading to change in the mental health service system in Arizona was a legal effort that supported the social movement and provided a political context within which planned change could be implemented. Litigation, in fact, was used to the fullest extent and proved to be a viable strategy for effecting reform, despite the fact that such efforts have met with something less than total success in other parts of the United States, where consent decrees and court orders have largely been ignored or have produced partial, ineffective results (2). However, Arizona's litigation, as described elsewhere (2), had some novel aspects. A class action suit representing chronically mentally ill persons had been filed and won by the

Arizona Center for Law in the Public Interest. The suit was based solely on state law, insisting on compliance with the existing statutes and avoiding federal law or Constitutional issues. It represented the combined efforts of lawyers and mental health professionals dedicated to the improvement of the system of care based on structural issues rather than solely on resources. The state's Division of Behavioral Health and the providers of services fought long and hard, arguing a lack of resources as the sole cause for the poor system of care. The plaintiffs argued instead, successfully, that the system was inefficient in the way it spent the dollars available.

The judge demonstrated in the language of his finding of facts, his conclusions of law, and his order that he understood the necessary principles and characteristics of an appropriate system of care. He ordered the state and the counties to abide by the statutes in a comprehensive yet not overly rigid court order (2). This action represented the careful and elaborate strategy of a team of lawyers and mental health professionals. It provided the impetus for an attempt at reformation through a legislated pilot project.

This action also helped demonstrate the ambivalence that was pervasive at the level of the executive branch of government. After supporting the effort at substantial reform as a demonstration of the intent by the Division of Behavioral Health to comply with the court order, the state appealed the decision to the higher courts. This strategy allowed the state to procrastinate and essentially slowed the advance of the reformation. For the legislative and executive branches, gaining a few years of respite through the lengthy appeal process was appreciable. For the social movement, it created a hiatus filled with self-doubt and discouragement. In 1988, the social movement received a strong impetus from the election of the most visible and active family member advocate to the Arizona House of Representatives (Eleanor Schorr). This turn of the tide culminated with a decision by the Arizona Supreme Court affirming the lower court's finding for the plaintiffs against the State of Arizona Division of Behavioral Health in March 1989. Since then, the governor and many influential legislators have expressed a firm commitment to comply with the court decision.

A blue ribbon task force has been appointed by the Governor and the legislature to propose a response to the court order. This task force is headed by a prominent member of the Tucson community who is also a family member and an active participant in the social movement to reform the system of care. By the spring of 1990, the task force will be in a position to substantially determine the structure and operation of the Arizona system of care for the severely mentally ill.

Oddly enough, at the same time that substantial progress is taking place, a rift has developed between most members of the social movement and the Center for Law in the Public Interest, which filed the lawsuit on behalf of the patients. The split originated from a disagreement over a reform of the civil commitment statutes proposed by the Alliance for the Mentally Ill and opposed by the Center for Law in the Public Interest in its advocacy role for patients. This disagreement has been mostly resolved, but it has strained relationships and has served to illustrate the fragility of a social movement from internal dissension. These unforeseen battles also underscore the difficulty in maintaining an effort at collective behavior involving participants with such disparate interests and multiple roles.

## RESULTS OF THE REFORM EFFORT

The combined action of the three forces used in Arizona (a social movement, planned change, and litigation) produced a pilot project that is currently operating. This project will provide data and a framework of reform when the legislature is forced to reexamine the system of care this year. This was brought about by including in the bill that established the pilot project a provision compelling the legislature to review the results of the pilot project in 1990 and, based on its findings, to contemplate a statewide implementation of the original model or an updated revision. The pilot project has been implemented in Tucson, Phoenix, and a rural area. It consists of a set of clinical teams that are assigned to 100 to 200 severely mentally ill patients. The teams are given control of all the resources to care for the patients in the form of per capita funding. They must purchase or provide directly all services from these funds and are solely responsible for the care of the patients assigned to them. An extensive study focusing on patient outcomes, family and consumer empowerment measures, and financial utilization is underway and has already begun to yield useful data (13).

The Division of Behavioral Health has spoken favorably of the pilot project's value and has indicated a plan to generalize its operation to most patients who are severely mentally ill in the state.

## CONCLUSIONS

The body of knowledge concerning the care of chronically mentally ill individuals has grown dramatically since the early years of deinstitutionalization (14–16). However, this knowledge has not been translated uniformly into correspondingly sophisticated, appropriate, and adequate systems of mental health care. Part of the difficulty has resided in the low priority given mental health care by national and state policy makers. Limited funding in many places has kept local mental health planners from introducing and implementing improved methods of service delivery.

Although limited allocations may serve as a partial explanation for failure to change in some places, this explanation is, by itself, not sufficient to explain a lack of progress. Proposed reforms, however, often proceed as if the key variable in the lack of progress were insufficient funding, the absence of an enlightened and persuasive program leader, or some other unilinear determinant, even though history tells us, if our common sense does not, that seeking to change only one variable at a time is at best a partial approach. We know that even in an era of ample funding like the 1960s and early 1970s, and even in states where creative mental health commissioners have come and gone (sometimes many times over), new initiatives have often fallen short of their intended goals.

The review of Arizona's unique experience reveals several factors that should be understood by those who would attempt to reform a mental health service system. It tells us, first of all, that the service system must respond to external realities and that changes within it are bound to be affected by, and must in turn have an effect on, the community's other institutions (17). Efforts at reform must be based on a sophisticated understanding of the politics and sociology of system change and well-founded knowledge of the particular community within which change is being proposed.

Second, the Arizona experience tells us that the pursuit of reform must allow for multivariate determinants of system change. In this review, I have identified three separate forces (a social movement, litigation, and planned change) that interacted to create a unique set of events for the State of Arizona. There are other critical variables that I have not discussed, but even this partial analysis lends a sense of the complexity of the process of reform.

Third, attempts to reform the mental health service system must proceed with a sensitivity to local realities. Neither service systems nor approaches to changing those systems can be cloned, even though many planners find it difficult to accept this reality. Indeed, attempts to import some other system into one's own community may have serious consequences. As Test and Stein (18) have noted, the system of care that they studied in Dane County, Wis., differed from more traditional systems along so many dimensions that it was difficult to sort out "which factors carry the greater part of the variance in accounting for the favorable results." Because of the complex uniqueness of systems of care, we may, in our ignorance, attempt to duplicate variables that are more obvious; in this we may easily create a no-win situation leading to frustration and demoralization (15).

Fourth, the Arizona experience tells us that reform in a system of care is an ongoing and longitudinal process. Although it is tempting to plan for a definitive reform and to report on its outcome, reality indicates that the process of evolution of a system of care is a never-ending endeavor. A system may progress, regress, or stall, depending on the existing conditions at the time. Even major and successful reform may become archaic or inoperable given time and neglect.

Fifth, the Arizona experience illustrates that, even under the best of circumstances, social movements must deal with dissension from within as well as from without. Throughout its history, the attempt at reform in Arizona has been one in which factionalism and internal disagreement have threatened its success and survival. In order to move forward, therefore, a collective action must focus its efforts on building enough consensus to overcome internal strife. Even slight shifts in the balance of internal power may redirect the social movement's longitudinal course and undermine its original purpose.

Finally, the experience in Arizona teaches us that we must be eclectic in our approaches to system reform. In this analysis of an evolving mental health service system, I have drawn from sources often ignored by mental health planners, i.e., literature from the fields of system theory, sociology, and social psychology. There is much to be learned from the experts in these areas.

Arizona's mental health service system represents a living and dynamic example of the complex nature of planned change. Only by understanding that complexity can we begin to control the process of system change effectively. Even when we have learned to modify our view of events to allow for multivariate determination, we shall still be faced with the need to learn about the conditions of what Bennis (19) called "changing" as opposed to "change," i.e., we shall still need to understand better how to anticipate the consequences of collective action instead of merely studying them retrospectively. In the area of mental health service system reform, our work is just beginning.

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# Partial Hospitalization: An Update

Susanna Parker, M.D., and James L. Knoll III, M.D.

*As a treatment modality for serious mental disorders, partial hospitalization has been proven to have therapeutic and economic advantages. However, it has relatively low utilization and poor third-party reimbursement compared to the more traditional outpatient and inpatient treatments. The authors provide a review and update of the definitions, historical development, models, staffing, and referral patterns of partial hospitalization. They comment on the role of the psychiatrist as a member of the multidisciplinary team in this treatment setting.*

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The concept of partial hospitalization for psychiatric disorders has evolved for more than 50 years. Its underlying premise is that most patients with serious mental disorders can be successfully treated in a less restrictive and less costly environment than an inpatient setting. At the same time, partial hospitalization should provide care which is more coordinated, intensive, comprehensive, and multidisciplinary than the outpatient treatment that is generally available. While the concept of partial hospitalization has flourished and the experience of mental health professionals supports its validity as an approach to treatment, utilization of partial hospitalization and third-party reimbursement for it remain poor in comparison with more traditional inpatient and outpatient treatment modalities (1, 2).

The literature reveals that partial hospitalization is as effective as inpatient care in treating psychotic patients who do not present an imminent risk of violence and that it is superior to outpatient treatment for chronic schizophrenic patients (1). To gain recognition and accountability, advocates of partial hospitalization have had to repeatedly address the following tasks: 1) defining partial hospitalization and clearing up confusing terminologies, 2) standardizing selection criteria and treatment models, 3) proving that partial hospitalization is a valid treatment modality with significant therapeutic and economic advantages, and 4) explaining why partial hospitalization has been poorly utilized.

Our purpose in this update is to offer a comprehensive review of partial hospitalization. After a discussion of the historical development, definitions, models, staffing, and referral patterns of partial hospitalization programs, we explore the reasons for the low utilization of this method of treatment.

## HISTORICAL DEVELOPMENT

The first "hospital without beds" was founded in Moscow in 1933 because of a shortage of beds and lack of funds (3). Thirteen years later, the first facility for partial hospitalization in the Western world was established in Montreal under the psychoanalytic auspices of Cameron (3). In the two decades that followed, biopsychosocial trends began to influence the mental health field, and the responsibility for patient treatment began to shift from physician to nonphysician professionals (4). The advent of psychotropic medications, concerns about burgeoning costs, and the civil rights movement spurred the passage of major legislation in the 1960s to deinstitutionalize the mentally ill. The Mental Retardation Facilities and Community Mental Health Center Construction Act of 1963 mandated the role of partial hospitalization in community mental health programs (4). Partial hospitalization programs were established because the federal government was attracted to their financial advantages and not necessarily because the psychiatric profession considered them a useful treatment modality (4).

A number of studies, however, have strongly supported the therapeutic as well as the fiscal advantages of partial hospitalization (5–13). Zwerling and Wilder (5) and Herz et al. (6) conducted studies in which patients were randomly assigned to partial hospitalization or inpatient settings. In those studies 66% and 22%, respectively, of the patients were found suitable for either treatment, and readmission rates for the inpatient groups were higher than for the partial hospitalization groups. In 1977 Herz et al. (7) published a controlled study in which 175 patients were randomly assigned to one of three treatment groups: a standard treatment (inpatient) group, a brief day hospitalization group (1 week as an inpatient followed by transitional

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day treatment), and a "brief-out" group (a short inpatient stay with outpatient follow-up and no day treatment). On a global rating of psychopathology and role functioning, the brief day hospitalization group had the best ratings and the standard treatment group the lowest. Over a 2-year period, the subsequent average inpatient days for the three groups were as follows: standard treatment group, 115.1 days; brief-out group, 46.8 days; brief day hospitalization group, 26.8 days. Similarly, in comparisons with outpatient care alone, most studies demonstrate that partial hospitalization is superior for chronic schizophrenic patients (14–17).

Cost-effectiveness, too, has been consistently demonstrated in comparison studies of partial hospitalization and inpatient treatment (1). Washburn et al. (18) and Endicott et al. (19) conducted studies which revealed that savings of up to 50% could be obtained when partial hospitalization was used to shorten the length of inpatient stay. Savings to third-party payers have been documented (1). One study (20) concluded that an insurance company could save money by offering insurance for day hospitalization on the same basis as for inpatient treatment.

Other investigators have documented the long-term cost-effectiveness of partial hospitalization (1, 21, 22). Fink et al. (23) concluded that the median cost of initial treatment in a day hospital was significantly lower than for full hospitalization, and after 1 year the initial lower costs were not offset by higher aftercare costs. In a study by Guidry et al. (24), it was shown that partial hospitalization can not only prevent full hospitalization but also can assist in decreasing the average length of stay when full hospitalization is unavoidable.

A wide variety and diversity of programs were established without clear definitions and guidelines in the 1960s and 1970s. In 1972 Glaser (25) summed up the criticism of that era: "Partial hospitalization programs have been inchoate, presenting no unified form or function to anyone. They have tried to be all things to all men and have succeeded only in not being utilized." In the late 1970s, partial hospitalization study groups organized formally and established the American Association for Partial Hospitalization (4). This is a multidisciplinary organization that now sponsors state and local chapters, the *International Journal of Partial Hospitalization*, and national meetings. Under its aegis, the concerns reflected in Glaser's comments were addressed; selection criteria for programs to serve homogeneous patient populations and formal standards and guidelines for partial hospitalization programs began to be developed.

## DEFINITIONS

Formal operational standards and guidelines, models for third-party coverage, and utilization review for partial hospitalization programs are now well established (4). In addition, in 1980 the Task Force on Partial Hospitalization of APA's New York County District Branch formulated the following definition of partial hospitalization:

> an ambulatory treatment program that includes the major diagnostic, medical, psychiatric, psychosocial, and prevocational treatment modalities designed for patients with serious mental disorders who require coordinated, intensive, comprehensive, and multidisciplinary treatment not provided in an outpatient clinic setting. It allows for a more flexible and less restrictive treatment program by offering an alternative to inpatient treatment. (26)

This definition can apply to day, evening, or weekend programs.

Patients suitable for partial hospitalization must be able to maintain themselves in the community at a minimally functioning level, present no immediate potential harm to themselves or others, and have a consistent place of residence (4). A partial hospitalization program should be conceived of as a separate, identifiable, organized unit serving as a link in the continuum of comprehensive mental health services offered in the community (4).

There are presently more than 1,000 partial hospitalization programs, either free-standing or affiliated with community mental health centers. The exact number remains uncertain because definitional ambiguities persist despite APA's efforts at clarification (1, 27). The variety and diversity of programs have produced various terminologies used by mental health professionals (4). "Day," "night," or "evening" hospital or "day treatment center" refers to those programs that include crisis intervention, diagnosis, and stabilization. "Day care" or "day care center" usually refers to programs that include training, rehabilitation, and maintenance (4). Partial hospitalization is clearly distinguished from psychosocial rehabilitation programs (self-help groups, Fountain House, Recovery, Inc., therapeutic social clubs, and lounge programs), which exist in nonmedical settings and are run by persons who are not mental health professionals (4).

## PROGRAM MODELS

In an attempt to match specific treatments to specific patient characteristics, Klar et al. (2) recommended three distinct but overlapping partial hospitalization models—intensive care, chronic care, and rehabilitation—with specific patient selection criteria for each. For each model, selection criteria are outlined under headings of relative indications, enabling factors, and relative contraindications (2).

The goals of the intensive care model are to decrease the length of inpatient stay and to be an alternative to inpatient hospitalization. It is designed to minimize the regressive and disruptive effects of inpatient hospitalization while still providing many of the services available on an inpatient unit. To facilitate the transfer of patients, when needed, intensive care programs should be situated close to inpatient services.

The chronic care model is characterized by modest expectations of patient improvement, high symptom tolerance, and a supportive, practical treatment approach. Klar et al. (2) noted that the "low-key therapeutic methods" in this model allow for a low staff-patient ratio. Chronic care programs are indicated for patients who would otherwise require custodial care, for patients who might deteriorate in the community, for patients who require a supervised environment, and for patients who require regular treatment but cannot tolerate a more active treatment program. Klar et al. noted that the stability of the patients' symptoms minimizes the need for the daily presence of a psychiatrist. Attendance requirements and length of stay are flexible in these programs.

The rehabilitation model is designed to provide an alternative to outpatient care for patients who have severe impairments in vocational or social performance. Patients are provided with strong support and structure. High therapeutic goals and expectations are set, and attendance is required, approximating a work environment.

Not all existing partial hospitalization programs serve patients separately in accord with the categories recommended by Klar et al. In some, a heterogeneous mix of acute and chronic patients is believed to enhance recovery and rehabilitation (1, 4, 28). Savings in cost can be obtained by serving mixed populations, since only one facility and staff are needed (1, 29). In addition, the effort to pursue precise selection criteria for specific partial hospitalization models may deter innovation and flexibility.

There has been much discussion about the use of auxiliary support facilities to complement ongoing treatment in partial hospitalization programs. Close ties with family and community are helpful in providing patients with a link to the real world. Geographical proximity to inpatient settings is advantageous when transfer is needed. The experiences of the Massachusetts Mental Health Center partial hospitalization service, which has a day hospitalization program in conjunction with a resident inn, suggest that their success in treating patients is often related more to the availability of social supports and a place to sleep than to the diagnosis or severity of illness (3, 12, 13). The University of Southern California's alternative hospitalization program consists of one entire floor (35 beds) of a 110-bed board and care home (3). The Massachusetts and California programs are treatment models that offer effective treatment with significant fiscal advantages compared to traditional inpatient programs. The Massachusetts Mental Health Center partial hospitalization service was given APA's Gold Award in 1985 for its highly efficient and cost-effective system (30).

Partial hospitalization has been used to provide specialty programs offering comprehensive treatment for children, adolescents, elderly persons, and neurotic, borderline, schizophrenic, diabetic, eating disorder, epilepsy, cancer, chronic disease, mentally retarded, and substance abuse patients (1). A review of the psychiatric literature on specialty day hospital programs indicates that there has been little progress in the development of these specialty areas, except in programs for children and adolescents (31–43). The growth in child and adolescent day hospitals appears to be stimulated by economic factors. We suspect that other specialty programs may follow in turn. Most of the specialty programs are relatively new, and sufficient time has not elapsed for the psychiatric literature to reflect adequately the growth and utilization of these programs.

## STAFFING AND REFERRAL PATTERNS

Staffing needs for partial hospitalization programs vary according to the type of services rendered. While most authors agree that a multidisciplinary team is needed to help develop a therapeutic alliance and sense of community early in the course of treatment (4), opinions vary with respect to who should lead the multidisciplinary team. The American Association for Partial Hospitalization standards recommend a director and a medical director in the upper echelons of the organizational structure. The medical director, a psychiatrist, may be the director as well; if not, he or she is responsible to the director (4). In practice there seems to be a dichotomy between the public and private sectors regarding leadership roles. In the private sector the medical model prevails; the medical director or the patient's psychiatrist leads the team and coordinates the patient's treatment. In this model nurses, aides, activity therapists, social workers, and psychologists function in the more traditional roles of testing and case management, and the psychiatrist is in more direct control of the patient's treatment plan. In the public sector the reverse is usually true. A social worker or a psychologist is frequently the program director, and social workers, psychologists, and nurses are the primary therapists. The physician is used mainly for medical evaluations and psychopharmacology and has less direct control over the patient's treatment plan. Fear of losing control of the patient to a system designed along nonmedical lines most likely decreases the referrals from psychiatrists.

Private-practice psychiatrists are rarely likely to refer patients to partial hospitalization programs (1). The limited role for physicians, as well as the smaller economic incentives, may account for the low referral rate from private psychiatrists. Fink and his associates (1, 44) determined that about half of the 90 referrals to their program over a 10-month period came from two physicians—one was the program chief and the other the program founder. For the rest, patients were referred by themselves, family, friends, or public facilities.

## DISCUSSION

Despite proven therapeutic and economic advantages, partial hospitalization has had relatively low utilization and poor third-party reimbursement. Reviewers have suggested that the most likely reasons for this underutilization are ambiguous definitions, lack of standardization, and clinician bias. These issues have been carefully weighed and resolved, for the most part, by authors who actively participate in successful partial hospitalization programs. In an age of deinstitutionalization and cost containment, partial hospitalization should have catapulted to the forefront of all the less restrictive alternative treatment modalities for the mentally ill. However, it has not.

The idea that psychiatrists do not frequently refer patients to partial hospitalization programs is a provocative one. The 1980s have brought new challenges regarding the role of the psychiatrist in the ever-growing movement toward community-based delivery of mental health care. Partial hospitalization continues to have low utilization for several reasons, all of them related to the fact that it is through a physician that most patients enter treatment. 1) Most psychiatrists have little or no training experiences in a partial hospitalization setting. 2) Full hospitalization is safer in a potential malpractice situation. 3) Psychiatrists can more easily recover third-party payments for full hospitalization. 4) The psychiatrist is easily accepted as the team leader and is more clearly in charge in a medically oriented inpatient setting than in a partial hospitalization setting, which tends to be "client" rather than "patient" oriented.

Traditional treatment modalities still offer a psychiatrist the least amount of risk, the greatest acceptance of his or her expertise to guide the treatment, and the most likely chances of reimbursement for services. Third-party payers' current reimbursement policies encourage full hospitalization, through economic incentives to both patient and physician. It is much more economically rewarding to fully hospitalize a patient. At best, partial hospitalization is usually reimbursed by using outpatient standards. Presently there are no *Current Procedural Terminology* codes specifically addressing day hospital care (45). There does seem to be a trend by mental health management firms toward utilization of day hospitals; however, it is still too early to tell whether this trend will become a pattern. In the past, third-party payers have avoided "new" alternatives to standard modalities because these have only added to, and not decreased, costs. Perhaps proposing a method of trade-offs of a specified number of day hospital days for each full hospital day would solve this dilemma and stimulate movement in this area.

It is our opinion that until more psychiatrists are trained in the use of partial hospitalization, more standardization of partial hospitalization takes place, and third-party payers economically direct patients and physicians toward partial hospitalization, the underutilization of this therapeutically and economically proven treatment modality will continue. The solution is simple; the implementation is complex.

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## Regular Articles

# Discriminating Borderline Personality Disorder From Other Axis II Disorders

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*The authors used the Revised Diagnostic Interview for Borderline Patients to assess 22 clinical features of 120 patients with borderline personality disorder and 103 control subjects with other axis II disorders. Four of the 22 features were common in but nondiscriminating for borderline disorder, 11 were discriminating for but nonspecific to borderline disorder, and seven were more specific to borderline disorder. The authors conclude that many clinical features thought to be indicative of borderline disorder are better viewed as personality disorder traits and that the seven more specific features, alone or in conjunction with one another, may be particularly useful markers for borderline personality disorder.*

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Numerous studies have detailed the characteristic clinical features of borderline personality disorder (1–29). Taken together, these studies have highlighted four areas of phenomenology as particularly characteristic of borderline patients: 1) intense, dysphoric affect, 2) transient cognitive difficulties, particularly those of a paranoid and dissociative nature, 3) widespread impulsivity, particularly of a physically self-destructive nature, and 4) intense, unstable relationships. Numerous studies have also shown that the clinical features of borderline personality disorder can be successfully discriminated from those of schizophrenic, depressed, nonpsychotic, and general psychiatric control subjects (2–7, 9–13, 16, 18, 20, 26, 29). However, the descriptive validity of borderline personality disorder will remain in question until it is proven that borderline patients can be reliably distinguished from patients with other forms of personality disorder, particularly the other disorders in the "dramatic" cluster of *DSM-III.*

Although numerous studies using control subjects with other axis II disorders have assessed the diagnostic efficiency of the *DSM-III* criteria set for borderline personality disorder (15, 22, 24, 25, 27, 28), only three studies have made any effort to determine if the clinical features of borderline patients were significantly different from those of patients with other forms of personality disorder (8, 14, 17).

One of these studies, by Sheehy et al. (8), compared the checklist ratings given to 45 outpatients clinically diagnosed as having borderline personality disorder with those given to a control group of 30 outpatients clinically diagnosed as having some other type of *DSM-II* personality disorder. Using a discriminant function analysis, they found that borderline patients had a higher score than the control subjects on nine of the 16 items studied: unusually strong feelings and impulses, trouble tolerating dysphoric affect, anhedonia, periodic paranoid distortions of reality, an episodic or chronic problem with impulse control, a history of promiscuity, episodic abuse of alcohol and/or drugs, a tendency to vacillate between idealizing and devaluing others, and difficulty maintaining a stable sense of self in a variety of external situations and internal mood states.

In the second study, Barrash et al. (14) administered the Diagnostic Interview for Borderline Patients (DIB) (30) to 18 inpatients with clinical diagnoses of borderline personality disorder and to a control group of 31 inpatients with clinical diagnoses of some other type of

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personality disorder. Using cluster analysis of the 29 summary statements of the DIB, these authors discriminated two types of borderline patients and found that both types of patients were significantly more likely than the control subjects to report three clinical features: depressive affect, self-mutilation, and manipulative suicide efforts.

In the third study, Frances et al. (17), using a 1-hour unstructured clinical interview, obtained diagnostic information on 76 outpatients. They found that the 26 patients who met *DSM-III* criteria for borderline personality disorder were significantly more likely to report each of the eight *DSM-III* borderline personality disorder criteria than were 50 control subjects with other axis II disorders.

For the study that will be described here, we used the 22 summary statements of the Revised Diagnostic Interview for Borderline Patients (DIB-R), a semistructured interview that can reliably distinguish clinically diagnosed borderline patients from patients with other axis II disorders (31), to assess the clinical features of borderline patients meeting DIB-R and *DSM-III* criteria and control subjects with other axis II disorders. This study builds on the design of the three earlier studies by incorporating all four of the following features. First, diagnostic assessments were made blind to clinical diagnosis. Second, assessments were made by using semistructured instruments of demonstrated reliability. Third, both inpatient and outpatient borderline patients and control subjects with other axis II disorders were studied. Fourth, control subjects meeting *DSM-III* criteria for a full range of axis II disorders were studied.

## METHOD

All subjects were either inpatients at McLean Hospital in Belmont, Mass., or outpatients at one of three clinics in the metropolitan Boston area (Revere Community Counseling Center, East Boston/Winthrop Community Counseling Center, and Bunker Hill Health Center in Charlestown). All patients at these facilities were considered eligible for inclusion if they 1) were between the ages of 18 and 40, 2) had normal or better intelligence, 3) had no history or current symptoms of a serious organic condition or major psychotic disorder (schizophrenia or bipolar disorder), 4) had been substance free for at least 10 days, and 5) had been given definite axis II diagnoses by the admitting physician or referring clinician.

Appropriate inpatients were identified by one of us (D.L.C.), who screened admission notes; appropriate outpatients were referred to the study by their therapists. One of us (M.C.Z.), who was blind to the patient's clinical diagnosis, then obtained written informed consent from each patient. She also evaluated the phenomenological status of each patient by administering the DIB-R and the Diagnostic Interview for Personality Disorders, a semistructured interview that reliably assesses the presence of the 11 axis II disorders described in *DSM-III* (32).

Subjects who met both DIB and *DSM-III* criteria for borderline personality disorder as assessed by the DIB-R and the Diagnostic Interview for Personality Disorders were included in the borderline group. The control group of subjects with other personality disorders comprised subjects who did not meet study criteria for borderline personality disorder but who did meet *DSM-III* criteria for some other type of axis II disorder as assessed by the Diagnostic Interview for Personality Disorders.

Between-group comparisons involving categorical data were computed by using the chi-square statistic corrected for continuity; between-group comparisons involving continuous data (age and socioeconomic status) were computed by using analysis of variance and the Newman-Keuls post hoc test of pairwise comparisons. The Bonferroni correction for multiple comparisons was applied where applicable.

## RESULTS

Overall, 253 patients were interviewed (148 inpatients and 105 outpatients). Thirty of these patients did not meet *DSM-III* criteria for an axis II disorder and were excluded from further analyses. One hundred twenty of the remaining patients had borderline personality disorder; 103 had other axis II disorders. The mean±age of the patients with borderline personality disorder was 27.3±6.3 years; the mean age of the patients with other personality disorders was 28.1±6.3 years. The mean socioeconomic status of the patients with borderline personality disorder was 3.6±1.3; that of the patients with other personality disorders was 3.6±1.1 (1=the highest status; 5=the lowest). The 120 borderline patients did not differ significantly from the 103 patients with other personality disorders on the variables of race, marital status, age (see table 1), and socioeconomic background. However, the borderline group contained a significantly higher percentage of women than the group of patients with other personality disorders (see table 1).

Of the 103 control subjects with other personality disorders, 66 (64.1%) met *DSM-III* criteria for a "dramatic" cluster disorder, 19 (18.4%) met *DSM-III* criteria for an "odd" cluster disorder, and 49 (47.6%) met *DSM-III* criteria for an "anxious" cluster disorder. (These percentages add up to more than 100% because some patients met criteria for disorders in more than one cluster.) The most common disorder was antisocial personality disorder: 53 (51.5%) of the control subjects with other personality disorders met *DSM-III* criteria for this very-near-neighbor disorder.

Table 2 shows the number of patients in each group who exhibited the clinical features detailed in the 22

**TABLE 1. Demographic Characteristics of Patients With Borderline Personality Disorder and Other Axis II Disorders**

| Characteristic | Patients With Borderline Personality Disorder (N=120) N | % | Patients With Other Axis II Disorders (N=103) N | % |
|---|---|---|---|---|
| Sex | | | | |
| Female | 88 | 73.3[a] | 38 | 36.9 |
| Male | 32 | 26.7 | 65 | 63.1 |
| Race | | | | |
| White | 118 | 98.3 | 102 | 99.0 |
| Other | 2 | 1.7 | 1 | 1.0 |
| Marital status | | | | |
| Ever married | 44 | 36.7 | 44 | 42.7 |
| Never married | 76 | 63.3 | 59 | 57.3 |

[a]Significantly higher than the percent of patients with other axis II disorders ($\chi^2=28.48$, df=1, $p<0.0001$).

summary statements of the DIB-R. At the Bonferroni-corrected alpha level of 0.002, a significantly higher percentage of borderline patients than control subjects with other personality disorders were judged to have exhibited 18 of these clinical features. Only four features—chronic feelings of helplessness/hopelessness/worthlessness/guilt, substance abuse/dependence, sexual deviance, and other (miscellaneous) impulsive patterns—failed to successfully discriminate borderline patients from those with other personality disorders.

Seventeen of the 22 summary statements also discriminated the 120 borderline patients from the 66 control subjects with other axis II personality disorders in the "dramatic" cluster at the Bonferroni-corrected level of $p<0.002$. Only substance abuse/dependence, sexual deviance, other (miscellaneous) impulsive patterns, stormy close relationships, and devaluation/manipulation/sadism failed to successfully distinguish these near-neighbor groups of patients. (The chi-square values and probability levels for these and subsequent comparisons not presented in tabular form are available from M.C.Z. on request.)

Because a significantly higher percentage of borderline patients than control subjects were women, two subanalyses to control for sex were also conducted. First, the rates of male and female borderline patients who exhibited each of the 22 summary statements of the DIB-R were compared: no significant differences were found at the Bonferroni-corrected level of $p<0.002$. The rates of male and female borderline patients and control subjects who exhibited each of these 22 variables were then compared. Despite the reduced power resulting from subdividing both of the original study groups, 10 summary statements successfully discriminated the female borderline patients and control subjects and nine successfully discriminated the male borderline patients and control subjects at the Bonferroni-corrected level of $p<0.002$. Eight of these clinical features successfully distinguished both male and female borderline patients from male and female control subjects: nondelusional paranoia, quasi-psychotic thought, self-mutilation, manipulative suicide efforts, abandonment/engulfment/annihilation concerns, dependency/ masochism, demandingness/entitlement, and countertransference problems/"special" treatment relationships. In addition, female borderline patients were significantly more likely than female control subjects to have a history of substance abuse/dependence and difficulty tolerating being alone, and male borderline patients were significantly more likely than male control subjects to have a history of stormy close relationships.

Six other summary statements successfully distinguished male and female borderline patients and control subjects at less stringent probability levels ($p<0.05$–$p<0.003$). Three of these clinical features successfully distinguished both male and female borderline patients from control subjects: chronic anger/frequent angry acts, devaluation/manipulation/sadism, and treatment regressions. In addition, female borderline patients were significantly more likely than female control subjects to report chronic feelings of helplessness/hopelessness/worthlessness/guilt and to have a history of sexual deviance (usually promiscuity) and other (miscellaneous) impulsive patterns. Male borderline patients were significantly more likely than male control subjects to have a history of chronic/major depression and to report chronic feelings of loneliness/boredom/emptiness and odd thinking/unusual perceptual experiences. All told, 16 clinical features were significantly more common in female borderline patients than female control subjects and 15 clinical features were significantly more common in male borderline patients than male control subjects.

## DISCUSSION

### *Affective Features*

Over 90% of the borderline patients in this study exhibited each of the five affective features studied. Over 75% of the control subjects with other personality disorders also exhibited each of these clinical features. However, borderline patients were significantly more likely than control subjects with other personality disorders to have exhibited each of these features except chronic feelings of helplessness/hopelessness/worthlessness/guilt. Earlier studies have found that feelings of depression, anger, and dysphoria were significantly more common among borderline patients than control subjects with other personality disorders (8, 14, 17). The results of this study confirm these findings. They also extend these findings by suggesting that borderline patients are more likely to report chronic feelings of anxiety than control subjects with other axis II disorders, a finding that, in turn, confirms the clinical impressions of numerous early observers of the borderline condition (33–37).

**TABLE 2. Patients With Borderline Personality Disorder and Other Axis II Disorders Who Showed Clinical Features in Summary Statements of the Revised Diagnostic Interview for Borderline Patients**

| | Patients With Borderline Personality Disorder (N=120) | | Patients With Other Axis II Disorders (N=103) | | | |
|---|---|---|---|---|---|---|
| Summary Statement | N | % | N | % | $\chi^2$ (df=1) | p |
| Affective features | | | | | | |
| Chronic/major depression | 115 | 95.8 | 78 | 75.7 | 17.55 | 0.0001[a] |
| Chronic feelings of helplessness/hopelessness/worthlessness/guilt | 116 | 96.7 | 89 | 86.4 | 6.54 | 0.01 |
| Chronic anger/frequent angry acts | 119 | 99.2 | 87 | 84.5 | 14.99 | 0.0001[a] |
| Chronic anxiety | 115 | 95.8 | 81 | 78.6 | 13.82 | 0.0002[a] |
| Chronic loneliness/boredom/emptiness | 120 | 100.0 | 89 | 86.4 | 15.17 | 0.0001[a] |
| Cognitive features | | | | | | |
| Odd thinking/unusual perceptual experiences | 85 | 70.8 | 35 | 34.0 | 28.82 | 0.0001[a] |
| Nondelusional paranoia | 111 | 92.5 | 62 | 60.2 | 31.42 | 0.0001[a] |
| Quasi-psychotic thought | 45 | 37.5 | 2 | 1.9 | 40.02 | 0.0001[a] |
| Impulsive features | | | | | | |
| Substance abuse/dependence | 91 | 75.8 | 65 | 63.1 | 3.69 | 0.05 |
| Sexual deviance | 51 | 42.5 | 42 | 40.8 | 0.02 | 0.90 |
| Self-mutilation | 58 | 48.3 | 9 | 8.7 | 39.48 | 0.0001[a] |
| Manipulative suicide efforts | 67 | 55.8 | 14 | 13.6 | 40.95 | 0.0001[a] |
| Other (miscellaneous) impulsive patterns | 119 | 99.2 | 93 | 90.3 | 7.51 | 0.006 |
| Interpersonal features | | | | | | |
| Intolerance of aloneness | 98 | 81.7 | 58 | 56.3 | 15.77 | 0.0001[a] |
| Abandonment/engulfment/annihilation concerns | 97 | 80.8 | 28 | 27.2 | 62.60 | 0.0001[a] |
| Counterdependency/serious conflict over help/care | 115 | 95.8 | 84 | 81.6 | 10.33 | 0.001[a] |
| Stormy relationships | 102 | 85.0 | 63 | 61.2 | 15.15 | 0.0001[a] |
| Dependency/masochism | 112 | 93.3 | 61 | 59.2 | 35.14 | 0.0001[a] |
| Devaluation/manipulation/sadism | 108 | 90.0 | 70 | 68.0 | 15.37 | 0.0001 |
| Demandingness/entitlement | 82 | 68.3 | 26 | 25.2 | 39.50 | 0.0001[a] |
| Treatment regressions | 53 | 44.2 | 15 | 14.6 | 21.54 | 0.0001[a] |
| Countertransference problems/"special" treatment relationships | 76 | 63.3 | 24 | 23.3 | 34.31 | 0.0001[a] |

[a] Application of the Bonferroni correction for multiple comparisons indicates statistical significance at $p<0.002$.

Perhaps more importantly, the results of this study also suggest that none of the affects studied is pathognomonic for borderline personality disorder. This result is not surprising, since clinical experience suggests that many types of patients with personality disorders suffer from serious affective symptoms. However, clinical experience also suggests that many borderline patients have a desperate need to convince others of the unique depth of their affective suffering. It may be that it is their eagerness to confide in others about their dysphoria rather than their actual level of dysphoria which sets borderline patients apart from those with other forms of personality disorder.

Taken together, the results of this study suggest that affective symptoms are ubiquitous in borderline patients. They also suggest that none of the affects studied is specific to borderline personality disorder.

### *Cognitive Features*

Over 35% of the borderline patients in this study exhibited quasi-psychotic thought, 71% exhibited odd thinking/unusual perceptual experiences, and 93% exhibited nondelusional paranoia. Odd thinking/unusual perceptual experiences and nondelusional paranoia were also common among control subjects with other personality disorders, but less than 2% of these control subjects exhibited quasi-psychotic thought. Nevertheless, all three of these clinical features were significantly more common among borderline patients than among control subjects with other axis II disorders.

Nondelusional paranoia has been found to be significantly more common among borderline patients than among control subjects with personality disorders (8). The results of this study confirm this finding. They also extend this finding by suggesting that odd thinking/unusual perceptions and quasi-psychotic thought are significantly more common among borderline patients than among control subjects with other axis II disorders. Both odd thinking/unusual perceptual experiences and nondelusional paranoia seem to be types of thought common to many forms of character pathology. However, quasi-psychotic experiences, which are defined as transient (less than 2 days' duration), circumscribed (involving only one or two areas of the patient's life), and/or atypical delusions and hallucinations (possibly reality based or totally fantastical in content), seem to be basically pathognomonic for borderline personality disorder. In this regard, it is particularly important to note that only one of the 19 control subjects with other personality disorders who met criteria for an "odd" cluster disorder exhibited this type of thought.

Taken together, the results of this study suggest that cognitive difficulties are extremely common among borderline patients. However, only quasi-psychotic experiences seem to be specific to borderline personality disorder and, as such, may prove to be a particularly useful marker for the disorder.

### *Impulsive Features*

Forty-three percent of the borderline patients in this study had a recent history of sexual deviance (most often promiscuity), 48% had physically mutilated themselves, 56% had made manipulative suicide efforts, 76% had abused alcohol, drugs, or both, and 99% had a history of some other type of impulsive pattern (e.g., eating binges, assaultive behavior, shoplifting). Promiscuity, substance abuse/dependence, and other (miscellaneous) impulsive patterns were also common among control subjects with other personality disorders and did not significantly distinguish these two groups of axis II patients. However, deliberately physically self-damaging acts and manipulative suicide threats and/or attempts were rare among control subjects with other personality disorders and were significantly more common among borderline patients than among those with other forms of personality disorder.

Earlier studies have found that both self-mutilating acts and manipulative suicide efforts were significantly more common among borderline patients than among control subjects with other personality disorders (14, 17). The results of this study confirm these findings, which suggest that borderline patients are virtually the only type of axis II patients who have a pattern of deliberately physically self-destructive acts: about three-quarters (70.8%) of our patients with borderline personality disorder but less than a fifth (17.5%) of our control subjects with other personality disorders had mutilated themselves and/or made manipulative suicide efforts. Earlier studies have also found that promiscuity, substance abuse/dependence, and other (miscellaneous) impulsive patterns were substantially more common among borderline patients than among control subjects with other personality disorders (8, 17). The results of this study contradict these findings. These differences are probably due, in part, to the more rigorous Bonferroni-corrected significance levels used in the present study. They are also probably due, in part, to the high percentage of control subjects with antisocial personality disorder in our study. This diagnostic group by definition is prone to substance abuse/dependence, promiscuity, and numerous other forms of outwardly directed impulsivity assessed in the current study.

Taken together, the results of this study suggest that most forms of impulsivity are not specific to borderline personality disorder. They also suggest that deliberately physically self-destructive acts are both the behavioral "specialty" of borderline patients and quite specific for the borderline diagnosis.

### *Interpersonal Features*

Over 80% of the borderline patients in this study had trouble tolerating aloneness, suffered from abandonment/engulfment/annihilation concerns, experienced conflicts about giving and receiving care, had stormy relationships, and had serious problems with dependency/masochism and devaluation/manipulation/sadism. In addition, 68% of these borderline patients were demanding and/or felt "entitled" in close relationships, 63% had been the object of a serious countertransference problem and/or formed an inappropriately close relationship with a care provider, and 44% had suffered a serious behavioral regression while in treatment. Although borderline patients were significantly more likely than control subjects with other personality disorders to have reported each of these problematic interpersonal patterns, over 50% of control subjects with other personality disorders reported difficulty tolerating aloneness, being strongly counterdependent, having intense, unstable relationships, and having close relationships marred by excessive dependency/masochism and devaluation/manipulation/sadism. In contrast, fewer than 30% of these control subjects reported profound concerns about being left, smothered, or destroyed in close relationships; being demanding or entitled in close relationships; serious countertransference difficulties; or severe treatment regressions.

Earlier studies have found that difficulty tolerating being alone and stormy relationships were significantly more common among borderline patients than among control subjects with other axis II disorders (8, 17). The results of this study confirm these findings. They also extend these findings by suggesting that each of the other seven interpersonal patterns studied is significantly more common among borderline patients than among control subjects with other axis II disorders.

Perhaps more importantly, these results also suggest that five of the nine interpersonal patterns studied—intolerance of aloneness, counterdependency, stormy relationships, dependency/masochism, and devaluation/manipulation/sadism—are exhibited by many patients with other types of character pathology. This finding, in turn, suggests that these patterns of interaction may be better thought of as personality disorder traits than as clinical features of borderline personality disorder per se.

Taken together, the results of this study suggest that the relationships of most borderline patients are fraught with multiple problems. However, only four of the interpersonal patterns studied seem somewhat specific for borderline personality disorder: abandonment/engulfment/annihilation concerns, demandingness/entitlement, treatment regressions, and the ability to arouse inappropriately close and/or hostile responses in professional caretakers. These interpersonal features may prove, alone or in conjunction with one another, to be useful markers for the borderline diagnosis.

### *Limitations*

The major limitation of this study is that the diagnostic determinations and the presence or absence of clinical features were not independently assessed. However, it should be noted that none of the clinical features assessed in the current study is necessary or sufficient to receive a DIB-R diagnosis of borderline personality disorder. Although one would expect most of the features studied to be more common among borderline patients than among control subjects with other axis II disorders, the exact pattern found was not dictated by the scoring algorithms of the DIB-R.

## CONCLUSIONS

Three types of clinical features were found in this study comparing criteria-defined borderline patients with patients with other axis II disorders: common but nondiscriminating features, highly discriminating but nonspecific features, and more specific or even pathognomonic features. Although the overall pattern of clinical features exhibited by borderline patients is probably more discriminating than any one feature taken alone, seven features were found to be somewhat specific to borderline personality disorder: quasi-psychotic thought, self-mutilation, manipulative suicide efforts, abandonment/engulfment/annihilation concerns, demandingness/entitlement, treatment regressions, and countertransference difficulties. This finding was particularly robust because these clinical features were found to be both highly discriminating and relatively specific for borderline personality disorder regardless of the control group used or the sex of the borderline patient.

Taken together, these results suggest that the diagnosis of borderline personality disorder has descriptive validity in that its clinical features can be clearly discriminated from other axis II disorders. They also suggest that borderline patients and patients with other axis II disorders share many clinical features commonly thought to be indicative of borderline personality disorder. These findings have important clinical implications given the propensity of many mental health professionals to label almost all affectively intense, impulsive, and interpersonally difficult patients as borderline (38). They may also have important implications for future research involving control subjects with other axis II disorders because criteria sets for borderline personality disorder that lack specificity may generate an unacceptably high rate of false positives.

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# Neuropathological Findings in Patients With Clinical Diagnoses of Probable Alzheimer's Disease

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*To assess prospectively the accuracy of standard antemortem clinical diagnostic criteria for Alzheimer's disease, post-mortem examinations were performed on 25 patients who had met* DSM-III *criteria for primary degenerative dementia and National Institute of Neurological and Communicative Disorders and Stroke criteria for probable Alzheimer's disease. Seventeen patients (68%) met neuropathological criteria for Alzheimer's disease. Two presenile-onset patients had diffuse neocortical senile plaques of insufficient number for definite Alzheimer's disease. Six patients had non-Alzheimer's disease diagnoses. Five of these six had presenile-onset dementia. These results suggest caution in the antemortem diagnosis of Alzheimer's disease in presenile-onset dementia.*

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Alzheimer's disease is the major cause of dementia in later life (1) and a disorder of increasing concern to psychiatry (2). Reliable antemortem diagnostic criteria are necessary for research and clinical purposes because the diagnosis of definite Alzheimer's disease depends on microscopic examination of the brain at autopsy. Although several sets of clinical criteria for the antemortem diagnosis of Alzheimer's disease have been proposed (3; *DSM-III*), neuropathological correlation studies continue to be needed for validation of these criteria. This study reports follow-up neuropathological examinations of 25 consecutively deceased patients given a prospective antemortem diagnosis of Alzheimer's disease according to specific clinical criteria.

## METHOD

The subjects were male inpatients on the Alzheimer's Disease Research Unit of the Psychiatry Service of the American Lake Veterans Administration Medical Center. All met *DSM-III* criteria for primary degenerative dementia as well as National Institute of Neurological and Communicative Disorders and Stroke criteria for probable Alzheimer's disease (3) in addition to other exclusionary criteria as described elsewhere (4). Evaluation included review of medical records, interview of the patient and caregivers, and extensive medical, neurological, and laboratory examinations, including CT scans, which confirmed the absence of focal intracranial pathology. Patients were evaluated and admitted when they were no longer able to function in the community. Therefore, we had not diagnosed these patients in the early stages of their dementing illnesses. Patients were admitted for longitudinal study until death.

General autopsy with brain removal was performed within 24 hours (usually within 5–6 hours) post-mortem. Brains were immediately placed on ice and later bisected in the midsagittal plane. The left half was fixed in 10% formalin for a minimum of 2 weeks for neuropathological study, and the right half was frozen at −70 °C for future biochemical analyses. The left cerebral hemisphere was sectioned coronally and the brainstem and cerebellum horizontally. In all cases, sections of the amygdala, hippocampus, parahippocampus, thalamus, hypothalamus, basal ganglia, cerebellum, midbrain, pons, and medulla and two or more sections of the frontal, parietal, temporal, and occipital cortices were examined. All sections were stained with hematoxylin and eosin, luxol-fast blue, PAS, the Holmes silver stain for axons, and the Holzer stain for astrocytes. In the three subjects who were without neurofibrillary tangles in the hippocampus (see Results), sections were stained with thioflavin S and Bielschowsky's stain, both of which are highly sensitive for neurofibrillary tangles (5). Sections from these three

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**TABLE 1. Age, Plaque Counts, and Post-Mortem Neuropathological Diagnoses of 25 Consecutively Deceased Patients Given the Antemortem Diagnosis of Probable Alzheimer's Disease**

| Patient, by Age at Onset of Dementia | Age at Onset (years) | Age at Death (years) | Neuropathological Diagnosis | Plaque Count[a] |
|---|---|---|---|---|
| Age 65 or before (presenile onset) | | | | |
| 4 | 62 | 68 | Alzheimer's disease | 20 |
| 6 | 61 | 70 | Alzheimer's disease | 30 |
| 9 | 63 | 72 | Alzheimer's disease | 13 |
| 10 | 60 | 68 | Alzheimer's disease | 13 |
| 11 | 59 | 66 | Alzheimer's disease | 15 |
| 16 | 57 | 70 | Alzheimer's disease | 20 |
| 13 | 48 | 61 | Alzheimer's disease | 22 |
| 17 | 53 | 67 | Alzheimer's disease | 19 |
| 19 | 61 | 76 | Alzheimer's disease | 20 |
| 25 | 57 | 67 | Alzheimer's disease | 19 |
| 3 | 51 | 58 | Probable Alzheimer's disease[b] | 21 |
| 12 | 52 | 57 | Possible Alzheimer's disease[c] | 6 |
| 22 | 57 | 62 | Possible Alzheimer's disease[c] | 7 |
| 1 | 54 | 61 | Corticostriatal gliosis | — |
| 20 | 60 | 73 | Parkinson's disease | — |
| 21 | 59 | 70 | Corticostriatal gliosis | — |
| 23 | 64 | 67 | Parkinson's disease | — |
| 24 | 48 | 63 | Pick's disease | — |
| Over Age 65 (senile onset) | | | | |
| 2 | 75 | 81 | Alzheimer's disease | 18 |
| 5 | 83 | 89 | Alzheimer's disease | 15 |
| 7 | 74 | 80 | Alzheimer's disease | 16 |
| 8 | 81 | 86 | Alzheimer's disease | 17 |
| 15 | 73 | 84 | Alzheimer's disease | 17 |
| 18 | 70 | 85 | Alzheimer's disease | 15 |
| 14 | 70 | 76 | Multiple system atrophy | — |

[a] Maximum number of plaques per square millimeter in a sampled neocortical field (7).

[b] Probable Alzheimer's disease without hippocampal neurofibrillary tangles and without other neuropathology.

[c] Possible Alzheimer's disease with plaque counts lower than necessary for diagnosis of Alzheimer's disease by Khachaturian criteria (7), without neurofibrillary tangles and without other neuropathology.

patients also were stained with antibody to the A-4 amyloid protein found in the senile plaques and amyloid angiopathy of Alzheimer's disease (6).

The neuropathological diagnosis of definite Alzheimer's disease used the criteria of Khachaturian (7), which are based on having an age-adjusted number of senile plaques per square millimeter in any sampled microscopic field. Multiple neocortical and hippocampal areas of high plaque density were scanned, and the areas of greatest plaque counts were recorded for diagnostic purposes. If the plaque count in one microscopic field encompassing 1 square millimeter (at 200 times magnification) exceeded the following age-adjusted criteria, the diagnosis of Alzheimer's disease was made: 2–5 for ages less than 50, 8 for ages 50 to 65, 10 for ages 66 to 75, and 15 for ages greater than 75. Patients were also diagnosed neuropathologically by the classic criteria of both numerous senile plaques and neurofibrillary tangles in neocortex and hippocampus (8).

## RESULTS

Twenty-five consecutively deceased patients who met antemortem criteria for probable Alzheimer's disease were autopsied. The mean±SD age at onset of dementia (by family report) was 62±9 years and mean duration of illness was 9±3 years. All patients were at stage 5 (moderately severe cognitive decline) or 6 (severe cognitive decline) on the seven-stage Global Deterioration Scale (9) at the time of admission. CT scans of all patients showed some degree of diffuse atrophy but did not show any other intracranial pathology.

The ages at onset of dementia and at death as well as neuropathological data of the 25 patients are presented in table 1. Seventeen patients fulfilled Khachaturian pathological criteria for Alzheimer's disease; one of these patients (patient 3) is classified as having probable Alzheimer's disease in the table. This patient was unusual in that no hippocampal neurofibrillary tangles were found, although neurofibrillary tangles were quite numerous in the entorhinal area; senile plaques were also numerous and widespread and were found in the entorhinal area and hippocampus, including the stratum moleculare, as well as in the neocortex. These plaques were positive for A-4 amyloid by immunohistochemistry. In two other patients with presenile-onset dementia (patients 12 and 22), senile plaques were less frequent and present only in the neocortex. Senile plaques in these two patients were positive for the A-4 amyloid protein but were not sufficient in number for a neuropathological diagnosis of definite Alzheimer's disease (3). Our neuropathological diagnosis for these patients was possible Alzheimer's disease. In patient 12, a few neurofibrillary tangles were present in the entorhinal area, but there were none in patient 22; otherwise, neurofibrillary tangles were absent from the hippocampus and neocortex of both patients.

Six patients did not have the neuropathological changes of Alzheimer's disease. Two patients (patients 1 and 21) had extensive cortical and basal ganglia degeneration manifested by marked neuronal loss and gliosis and were given the diagnosis of corticostriatal degeneration. One patient with multiple system atrophy (patient 14) had widespread gliosis of the basal ganglia, thalamus, substantia nigra, tectum, and tegmentum of the midbrain, dentate nucleus, and red nucleus but no hippocampal or neocortical abnormalities. Two patients (patients 20 and 23) had the neuropathological features of Parkinson's disease, one (patient 23) with Lewy bodies and the other (patient 20) without Lewy bodies but with severe neuronal loss and gliosis of the substantia nigra. One patient (patient 24) had the typical neuropathological features of Pick's disease (10).

The mean±SD age at onset of the 18 patients with presenile-onset dementia was 57±5 years; that of the seven patients with senile-onset dementia was 75±5 years. All but one of the six patients with non-Alzheimer's disease neuropathological diagnoses and both patients with possible Alzheimer's disease had presenile-onset dementia (at age 65 or before). Thus, 11 (61%) of the 18 patients with presenile-onset dementia met the Khachaturian criteria for Alzheimer's disease (7). Given that one presenile-onset patient who met the Khachaturian criteria had neurofibrillary tangles limited to the entorhinal cortex and absent from the hippocampus and neocortex, only 10 (56%) of the 18 presenile-onset patients had the full classic neuropathological features of Alzheimer's disease. In contrast, six (86%) of the seven senile-onset patients met the Khachaturian criteria and also had the full classic neuropathological features of Alzheimer's disease. The one patient with senile-onset dementia who did not have Alzheimer's disease had the earliest age at onset (70 years) of the senile-onset group.

None of the 25 patients had large or extensive cerebral infarctions. One patient (patient 6) had a small cystic infarction in the left occipital lobe. Another (patient 7) had several small old lacunar infarctions of the putamen and thalamus, and a third (patient 11) had a small old cystic infarction of the cerebellum.

## DISCUSSION

The 68% neuropathological confirmation rate of Alzheimer's disease in this sample based on the Khachaturian criteria is lower than the neuropathological confirmation rates reported in other series in which most patients had senile-onset dementia (11–14). In fact, Morris et al. (15) recently reported a 100% neuropathological confirmation rate in 26 patients diagnosed antemortem as having senile-onset Alzheimer's disease. It appears from our data that the neuropathological confirmation rate of Alzheimer's disease may be lower in patients with presenile-onset dementia. Although with our small sample the differences between groups were not statistically significant ($\chi^2=2.00$, df=1), only 56% of our presenile-onset patients had the full classic Alzheimer's disease findings of both numerous senile plaques and numerous neurofibrillary tangles in the neocortex and hippocampus (8). In contrast, 86% of our senile-onset patients had these full classic features of Alzheimer's disease. These findings suggest that presenile-onset subjects selected for clinical studies using standard clinical diagnostic criteria for Alzheimer's disease may not be a neuropathologically homogeneous group.

When the patients described in this report were examined, the Holmes silver stain was the standard stain used in our laboratory to detect senile plaques and neurofibrillary tangles. This stain is less sensitive than but as specific as the Bielschowsky and thioflavin S stains (unpublished observations). Therefore, any subject meeting Khachaturian plaque count criteria for probable Alzheimer's disease with the Holmes stain would also meet criteria with the more sensitive Bielschowsky and thioflavin S stains. The subjects who were diagnosed as having possible Alzheimer's disease and/or who did not have neurofibrillary tangles were also studied with the more sensitive stains; this did not change the histologic findings.

The absence of hippocampal neurofibrillary tangles in three patients with presenile-onset dementia is difficult to explain. In an autopsy series of Alzheimer's disease patients in whom 30% lacked neurofibrillary tangles in the neocortex, substantial numbers of neurofibrillary tangles were always found in the hippocampus (16). Because of this constant hippocampal involvement, Ball et al. (17) suggested that Alzheimer's disease may also be called "hippocampal dementia." Certainly for patient 3, in whom tangles were numerous in the entorhinal area and senile plaques were widespread and present also in the stratum moleculare of the hippocampus, the diagnosis of Alzheimer's disease appears to be justified. Hyman et al. (18) hypothesized that the entorhinal area is the primary site of neuronal degeneration in Alzheimer's disease and that there are secondary changes in the hippocampus manifested by senile plaques in the stratum moleculare. It is possible that patient 3 and the two patients given the neuropathological diagnosis of possible Alzheimer's disease may not have expressed hippocampal neurofibrillary tangles because of very early onset (ages 51, 52, and 57) and the brief clinical courses of their illnesses (7, 5, and 5 years, respectively). However, our experience and that of others indicate an inverse relationship between age at onset and density of neurofibrillary tangles in Alzheimer's disease (19).

Our antemortem diagnostic criteria excluded multi-infarct dementia. Although three patients (patients 6, 7, and 11) had infarcts that were small both in extent and by location, the infarcts were unlikely to have contributed substantially to these patients' severe dementia. This 17% incidence rate of small infarcts in our Alzheimer's disease patients was lower than that reported in both Alzheimer's disease patients and nondemented elderly subjects in the classic study of Tomlinson et al. (20). Because only the left half of the brain was available for our neuropathological examination, it is possible that the number of infarcts and volume of affected tissue were underestimated. In the study of Wade et al. (13), approximately one-fourth of Alzheimer's disease patients had infarcts at autopsy that were judged to be clinically unimportant.

Three patients with presenile dementia of long duration, clinically similar to Alzheimer's disease, had neuronal loss and gliosis in multiple brain regions as their major neuropathological findings. Other investigators have reported similar patients with a clinical course typical of Alzheimer's disease, who at postmortem examination had findings limited to neuronal loss and gliosis. Sulkava et al. (11) reported two patients with hippocampal neuronal loss and gliosis as well as subcortical gliosis, and Wade et al. (13) reported similar patients. Ball et al. (17) reported two patients who met *DSM-III* criteria for primary degenerative dementia whose predominant neuropathology was neuronal loss and gliosis in the hippocampus. Bowen et al. (21) reported that two of seven patients with progressive presenile-onset dementia had no histologic evidence of Alzheimer's disease on cortical biopsy. Neumann and Cohn (22) reported four patients with insidious progressive dementia of 3 to 17 years' duration, with pronounced subcortical gliosis at autopsy. They proposed the term "primary subcortical gliosis" for this syndrome.

Two other patients with only the neuropathological changes of Parkinson's disease had progressive dementia of long duration with the appearance of extrapyramidal signs only in the later stages of their dementing illnesses. Although dementia is common in Parkinson's disease, it usually follows the appearance of motor signs and symptoms (23). Wade et al. (13) reported a patient given a clinical diagnosis of Alzheimer's disease who had non-Lewy body Parkinson's disease. Sulkava et al. (11) described a similar patient who proved to have Parkinson's disease with Lewy bodies rather than Alzheimer's disease. This patient also did not develop extrapyramidal signs until late in her dementing illness. Our findings lend further support to the hypothesis that the lesions of Parkinson's disease alone are sufficient for the development of dementia in susceptible patients (24).

The frequency of non-Alzheimer's disease neuropathological diagnoses in our presenile-onset dementia patients who met clinical antemortem criteria for probable Alzheimer's disease emphasizes the importance of long-term follow-up and eventual autopsy diagnostic confirmation for such patients, particularly those who participate as subjects in clinical research. With this problem in mind, we examined the neuropathological diagnoses of Alzheimer's disease patients who had participated in our neuroendocrine studies (4, 25, 26). Fortunately, only one of the patients with non-Alzheimer's disease diagnoses had participated in these studies, and exclusion of this patient's data did not alter our results or conclusions. Our findings also reinforce the importance of neuropathological diagnosis for the definition of familial Alzheimer's disease pedigrees for genetic linkage analysis. Presenile-onset Alzheimer's disease patients have been prominently represented in such studies (27).

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# Antisocial Personality Disorder in Patients With Substance Abuse Disorders: A Problematic Diagnosis?

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*The authors' literature review suggests that the relationship between antisocial personality disorder and substance abuse is complex and not yet fully understood. The confusion regarding the relationship between the disorders may be magnified by the emphasis in* DSM-III *and* DSM-III-R *on behavioral criteria and their failure to require that antisocial behaviors exist independently of substance abuse. The* DSM-III *and* DSM-III-R *formulations of antisocial personality disorder may encompass two subgroups of substance abusers—"true" psychopathic individuals and symptomatic psychopaths with little psychopathy. Psychoneurotic symptoms and favorable treatment responses might be found more often in the latter group.*

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Antisocial personality disorder is a psychiatric diagnosis frequently seen in patients with substance abuse disorders. Studies using *DSM-III* criteria have shown the incidence rate of antisocial personality disorder to be about 40% to 50% in samples of male alcoholic patients (1, 2) and male opiate addicts (3, 4). This high incidence rate underscores the importance of understanding the impact of antisocial personality disorder on substance abuse. However, a critical review of the literature reveals apparent problems in the application of the diagnosis of antisocial personality disorder, particularly with regard to substance abusers.

## ORIGIN OF THE DIAGNOSIS OF ANTISOCIAL PERSONALITY DISORDER

The *DSM-III* and *DSM-III-R* criteria for antisocial personality disorder focus on behavioral patterns rather than underlying personality dynamics. Presumably, the thought of the formulators of *DSM-III* and *DSM-III-R* was that personality features would be indirectly reflected in antisocial behavior. The primarily behavioral conceptualization of *DSM-III* and *DSM-III-R* was greatly influenced by Robins's study of delinquent boys (5, 6). Robins found that conduct problems in childhood were the best predictors of adult antisocial behavior; that is, she found a great deal of continuity between childhood and adulthood antisocial behavior and concluded that this reflected a unitary syndrome. The behavioral predictors she identified formed the basis for the *DSM-III* and *DSM-III-R* criteria for antisocial personality disorder.

To receive the diagnosis of antisocial personality disorder, an individual must show antisocial behaviors before the age of 15 and must manifest three of a possible 12 antisocial behaviors (e.g., truancy and lying) before the age of 15. The individual who meets these criteria before age 15 must also engage in four of a possible 10 adult antisocial behaviors, such as an inability to sustain interpersonal relationships, failure to conform to societal norms, and failure to honor financial obligations. It should be pointed out that the *DSM-III* and *DSM-III-R* criteria for antisocial personality disorder reflect a prototypic approach to diagnosis. In this type of system, various combinations of behaviors allow the individual to meet the diagnostic criteria (7). In other words, there are no critical items. Thus, although *DSM-III-R* includes some items that attempt to tap personality features such as the ability to maintain a monogamous relationship, such items are not considered essential features of the diagnosis. The majority of items seem to be more descriptive of antisocial behaviors than of underlying personality features.

Other diagnostic systems, such as that of Guze (8), the Feighner criteria (9), and the Research Diagnostic Criteria (RDC) (10), also rely heavily on behavioral indicators in making the diagnosis of antisocial personality disorder. The RDC are perhaps the most stringent in that they require markedly impaired interpersonal relationships and independence of the antisocial behaviors from substance abuse.

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## PSYCHOPATHY: A CONFLICTING CONCEPTUALIZATION

Although we tend to think of the term "psychopath" as synonymous with antisocial personality, until the 1930s it was used as a generic label referring to several different types of pathology thought to result from some general form of constitutional weakness (11–13). More than 150 years ago, Pritchard (14) speculated that the behavior of some antisocial individuals resulted from constitutional deficits but that other individuals manifested antisocial behaviors only in response to transient stress. This notion resurfaced in the psychoanalytic understanding of antisocial personality and antisocial behavior. Both *DSM-I* and *DSM-II* descriptions of the criteria for antisocial personality disorder were based on this psychoanalytic conceptualization. This perspective is perhaps best exemplified in the highly influential work of Cleckley (15). In describing a psychopathic personality type, Cleckley emphasized such dynamic features as the inability to experience guilt or remorse, anxiety, and loyalty; the inability to form meaningful, lasting relationships; and the manipulation of others to serve one's own ends. Cleckley and other psychoanalytic writers (16, 17) emphasized that some psychopathic individuals do not get into trouble with the law but still demonstrate the underlying psychopathology of the disorder.

Like Pritchard (14), a number of psychoanalytic writers divided individuals who engaged in antisocial behaviors into two groups: an antisocial group whose deviant behavior was believed to be an expression of constitutional deficits or more severe pathology and an antisocial group whose behavior they considered to be an expression of neurotic conflict (18–21). Individuals in the former group have been called "true psychopaths" (18, 19) or "idiopathic psychopaths" (21), and individuals in the latter group have been given a variety of labels such as "neurotic characters" (18, 19) or "symptomatic psychopaths" (21).

Karpman (21) strongly admonished that the presence of antisocial behavior should not in itself be sufficient for the diagnosis of idiopathic psychopathy because antisocial behavior is present in individuals with many other disorders and the prognostic implications for the latter form of psychopathy are qualitatively superior to that of the former. This conceptualization of the true (idiopathic) psychopath can be seen in the *DSM-I* and *DSM-II* formulations, including the admonishment against including symptomatic psychopaths in this diagnostic category. This admonishment was obviously not followed in the *DSM-III* and more recent *DSM-III-R* formulations of antisocial personality disorder.

## CRITICISMS OF *DSM-III* CRITERIA

When compared with the other personality disorders, the establishment of the *DSM-III* criteria for antisocial personality disorder resulted in the most controversy (22). The fundamental reason for the adoption of the behavioral operationalization of antisocial personality disorder by the *DSM-III* committee on personality disorders was its concern with reliability and standardization across the psychiatric community. However, Vaillant (23) has argued that, in taking this approach, validity may have been sacrificed at the altar of reliability.

Not surprisingly, much of the criticism against the criteria for antisocial personality disorder was focused on the extent to which the diagnosis emphasizes socially deviant behaviors rather than an underlying dynamic personality structure. For example, one of the most outspoken critics of the *DSM-III* criteria for antisocial personality disorder, Theodore Millon (24), noted in his response to the 1978 draft version of the *DSM-III* criteria that "the write-up fails to deal with personality characteristics at all, but rather lists a series of antisocial behaviors that stem from such characteristics" (p. 182). Millon felt that the criteria for antisocial personality disorder gave undue prominence to the delinquent or criminal expression of the personality. Frances (22) raised similar criticisms and stated that "it would be more useful to have criteria that distinguish those criminals who are capable of loyalty, anxiety and guilt from those who are not, since the behavior and management of each group are likely to be quite different" (p. 1053). Hare (25) criticized the triviality of the antisocial acts (such as childhood thefts, lying, and truancy) that are used to diagnose antisocial personality disorder in *DSM-III.*

Partly in response to these types of criticisms, the antisocial personality disorder criteria were changed somewhat in *DSM-III-R*. Under the adult criteria, an item to express the concept of an absence of guilt or remorse was added. This, however, is included in a list of 10 adult behaviors, four of which must be manifested. An inability to experience guilt and other core personality features are thus not prerequisites for the disorder.

Although the criteria tap some of the personality dynamics associated with the true psychopath, such as difficulties in interpersonal relationships, none is considered essential for the diagnosis. As indicated, *DSM-III* and *DSM-III-R* use a prototypic approach that allows for and may result in numerous permutations of antisocial behavior patterns. Since the criteria do not differentially weight items directly assessing underlying personality dynamics, it is possible that both idiopathic and symptomatic psychopathic individuals are encompassed within the *DSM-III* and *DSM-III-R* diagnosis of antisocial personality disorder.

## SHOULD ANTISOCIAL PERSONALITY DISORDER BE INDEPENDENT OF SUBSTANCE ABUSE?

The question of the relationship between the diagnosis of substance abuse and the diagnosis of antisocial personality disorder introduces particular problems because substance abuse is often considered an antisocial behavior that in and of itself can induce specific behavioral problems, such as irresponsibility, impulsivity, and criminality related to obtaining drugs. Although such behaviors may be consequences of substance abuse, they are also considered to be reflective of antisocial personality disorder. A point of conflict, then, is whether antisocial behaviors can or should be viewed as independent of substance abuse.

This source of controversy is reflected in the differences between *DSM-III* and *DSM-III-R* criteria and RDC (10) for antisocial personality disorder. *DSM-III* and *DSM-III-R* accept antisocial behaviors in the context of substance use as evidence of antisocial personality disorder as long as the individual meets the criteria for childhood antisocial personality disorder. In other words, substance use is viewed as an expression of a general syndrome of global antisocial personality disorder involving poor impulse control, inability to form mature interpersonal relationships, and lack of guilt. On the other hand, the RDC, a diagnostic system sometimes used for research purposes, emphasize that antisocial behaviors may evolve as a result of or be exacerbated by a substance use disorder. The RDC specifically require that antisocial behaviors must not be a result of substance abuse.

Because of these differences in the diagnostic systems, a substantially larger percentage of substance abusers are diagnosed as having antisocial personality disorder when the *DSM-III* criteria are applied than when RDC are applied. For example, Woody et al. (4) found that although 45% of the opiate addicts in their psychotherapy outcome study met *DSM-III* criteria for antisocial personality disorder, only 19% were diagnosed as having antisocial personality disorder according to the RDC. In another study of 533 opiate addicts, Rounsaville et al. (26) found that 54% of the subjects were diagnosed as antisocial according to *DSM-III* criteria, but only 27% were similarly diagnosed according to the RDC. Most (96%) of the patients who received the RDC diagnosis also met the *DSM-III* criteria, but a much lower percentage (44%) of the patients who met the *DSM-III* criteria also met the RDC. Rounsaville et al. (26) labeled those patients for whom antisocial activities were independent of the need to obtain drugs (basically those who received the RDC diagnosis) "primary antisocial addicts," and they labeled as "secondary antisocial addicts" those for whom antisocial activity was directly related to drug use. The primary antisocial group reported more childhood behavioral disruptions and more severe psychopathology than the secondary antisocial group. Although no data were presented on the treatment outcomes of the two groups, the authors speculated that the secondary antisocial addicts might show a better treatment response.

## RELATIONSHIP BETWEEN ANTISOCIAL PERSONALITY DISORDER AND SUBSTANCE ABUSE

Although some confusion regarding our understanding of the relationship between antisocial personality disorder and substance abuse is reflected in the differences between the RDC and *DSM-III* and *DSM-III-R* criteria, it is clear from most of the literature that there is at least a general association between substance abuse and antisocial personality characteristics (27). A number of authors have speculated that environmental and genetic factors, alone and in combination, should be considered in understanding the etiology of both disorders. For example, Akiskal et al. (28) suggested that alcoholics with antisocial personality disorder may represent a subset of a "character spectrum disorder" that has genetic determinants. Although more sophisticated methodologies are needed before definitive conclusions can be drawn about genetic and environmental contributors to substance abuse (29), there are some data supporting the idea that genetic and environmental factors play a role in the etiology of both antisocial personality disorder and substance abuse disorders (30–32). In 1987 Cloninger (33) presented evidence that a form of early-onset alcoholism, designated type-2 alcoholism, is associated with childhood and adolescent antisocial behaviors and paternal criminality.

## "PSYCHONEUROTIC" SYMPTOMS IN SUBSTANCE ABUSERS WITH ANTISOCIAL PERSONALITY DISORDER

Affective disorders have been hypothesized to be related to the initiation of both substance abuse and antisocial behaviors. Numerous workers have described "psychoneurotic" symptoms such as depression and anxiety in substance abusers with antisocial personality disorder. For example, Whitters et al. (34) noted that a number of researchers (35–38) have found that depression and antisocial personality disorder frequently occur together in alcoholics. It should be noted that these studies used criteria different from those of *DSM-III* and *DSM-III-R*. A number of more recent studies have found that many substance abusers with antisocial personality disorder also qualify for a lifetime diagnosis of major depression or an anxiety disorder (2, 4, 39, 40). Whitters et al. (34, 41) distinguished between alcoholics with antisocial personality disorder who reported many symptoms of depression and those who did not, finding that the former were more likely to report other psychopathology such as symptoms of anxiety disorders. Akiskal et al. (28) noted that, in some instances, antisocial behavior may actually be an expression of an affective disorder. A similar idea has been advanced regarding antisocial behaviors that begin in adolescence. That is, some clinicians have suggested that conduct disorders and antisocial behavior in childhood and adolescence frequently mask an underlying depression (42, 43).

Interestingly, the coexistence of depression in antisocial patients has often been considered a predictor of positive treatment response. Lion (44) linked the occurrence of depression in the psychopath to a more positive treatment outlook. Similarly, Rounsaville et al. (26) stated that "an important issue regarding the diagnosis of antisocial personality disorder in addicts is the extent to which this subgroup can become involved in treatment due to the motivation provided by painful affects."

It might be considered surprising to find so many psychoneurotic symptoms in subjects with antisocial personality disorder, unless we again consider the possibility that antisocial personality disorder may include both the true or idiopathic psychopath, who shows both antisocial behavior and antisocial character structure (15), and the symptomatic psychopath, who exhibits antisocial behavior but who also shows signs of guilt, remorse, and interpersonal attachment. This consideration may be particularly pertinent in the case of substance abusers, where early involvement with alcohol and/or drugs may promote a surge of antisocial behaviors that qualify them for a behaviorally based diagnosis of antisocial personality disorder. It is possible that such individuals would have neurotic symptoms and an underlying character structure that is different from that of true psychopaths. A hypothesis worthy of consideration is that the current diagnosis of antisocial personality disorder in substance abusers includes both idiopathic and symptomatic psychopaths.

Studies by Hare (25) and Harpur et al. (45) suggest that this hypothesis might extend to the more general group of patients with antisocial personality disorder. These researchers found that prisoners with high scores on a measure of true psychopathy (the Psychopathy Checklist) showed lower levels of anxiety than those with lower scores. High scores on this measure were predictive of recidivism, but the *DSM-III* diagnosis of antisocial personality disorder had little predictive validity. Although these investigations were not conducted with substance abusers, they are supportive of the hypothesis that there is heterogeneity among patients who are diagnosed as having antisocial personality disorder.

## TREATMENT OUTCOME OF SUBSTANCE ABUSERS WITH ANTISOCIAL PERSONALITY DISORDER

There is a common belief that idiopathic psychopathic individuals respond poorly to conventional treatments. Uniformly poor outcomes are usually also projected for substance abusers who meet diagnostic criteria for antisocial personality disorder (39, 46). However, this viewpoint has not taken into account possible distinctions between idiopathic and symptomatic psychopaths. The primary question is whether antisocial personality disorder is a uniformly negative predictor of treatment outcome or whether the idiopathic/symptomatic distinction is pertinent to treatment response.

Relatively few systematic studies have specifically examined the treatment outcome of substance abusers with antisocial personality disorder. Only one study (4) has found their treatment outcomes to be worse than that of substance abusers with other psychiatric conditions (depression). Much of what has been concluded concerning the poorer treatment response of antisocial substance abusers appears to be based on the indirect evidence of greater severity of the addiction of the substance abuser with antisocial personality disorder (39, 46) and findings that the presence of antisocial personality or any other psychiatric diagnosis in substance abusers is associated with poorer treatment outcome (2, 47).

For example, Penick et al. (2) reported that three subgroups of alcoholics who qualified for a lifetime diagnosis of antisocial personality disorder, major depression, or mania/depression were doing more poorly than alcoholics who had no additional psychiatric diagnoses. Since these subgroups were also doing more poorly at intake and there was no apparent effort in the statistical analyses to take such baseline differences into account, it is not clear that the subgroups with additional psychopathology benefited less from treatment. Further, no evidence was provided that the subgroup with antisocial personality disorder responded more poorly than the other two subgroups with additional psychiatric diagnoses.

Schuckit (48) found that male alcoholics with a diagnosis of drug abuse or antisocial personality preceding the onset of alcoholism had poorer outcomes 1 year after treatment than did those whose alcoholism came before their psychiatric disorder. Rounsaville et al. (47) found that alcoholics who qualified for an additional diagnosis of antisocial personality disorder, drug abuse, major depression, or other psychiatric disorder did more poorly at 2.5-year follow-up than a group of alcoholics with no additional psychiatric diagnoses. These investigators were not able to conclude that the group with antisocial personality disorder fared more poorly than the groups with other additional psychiatric disorders. However, in other studies, Rounsaville et al. (3, 40) reported that opiate addicts with antisocial personality disorder had more legal, employment, and psychosocial problems at follow-up than opiate addicts with no additional psychiatric diagnoses.

The most pertinent findings to date on treatment response in substance abusers with antisocial personality disorder have been those of the University of Pennsylvania–Veterans Administration psychotherapy study, reported by Woody et al. (4), which revealed that methadone-maintained opiate addicts with an additional psychiatric diagnosis of antisocial personality disorder were doing more poorly at 7-month follow-up than groups of methadone-maintained patients who had no additional psychiatric diagnosis, an additional lifetime diagnosis of major depression (not necessarily current), or antisocial personality disorder plus a lifetime diagnosis of depression. Although the group with only antisocial personality disorder did not show a response to psychotherapy, the substance abusers with antisocial personality disorder who also met the criteria for major depression showed a positive treatment response. This finding suggests that some substance abusers with a diagnosis of antisocial personality disorder, perhaps the symptomatic psychopaths, can benefit from individual psychotherapy.

In discussing the potential reasons for the different therapeutic responses of depressed and nondepressed subgroups of patients with antisocial personality disorder, Woody et al. (4) speculated that "perhaps more than any other aspect of the sociopathy syndrome, the paucity of and superficiality of relationships may be the most negative contributor" to the poor outcome for the "pure" antisocial addicts (p. 1085). In other words, they felt that the poor object relations of this subgroup prevented them from benefiting from psychotherapy. As a partial attempt to address this possibility, we reanalyzed the University of Pennsylvania–Veterans Administration data and found that within the group of substance abusers with antisocial personality disorder there was a relationship between the ability to form a positive relationship with a therapist and treatment outcome (49). Unfortunately, the relatively small sample size prohibited an analysis of potential interaction effects among depression, antisocial personality disorder, and the ability to form a positive therapeutic relationship in regard to treatment outcome. Our findings reinforce the viewpoint that there is substantial heterogeneity among substance abusers with antisocial personality disorder with respect to ability to benefit from treatment.

## IS PSYCHOPATHY A VIABLE CONCEPT?

We presume that the subjective and complex nature of the judgments required by Cleckley (15) for the determination of psychopathy (e.g., unreliability, lack of remorse or shame, inability to empathize) resulted in their virtual abandonment and replacement by an emphasis on antisocial behaviors. However, Hare (25, 50) has developed a reliable and stable measure of psychopathy based directly on Cleckley's conceptualization and specific features. This measure, the Psychopathy Checklist, uses a semistructured interview format in conjunction with information from records and can be completed by college student raters (51). Presumably, the Psychopathy Checklist can be used in conjunction with or independently of *DSM-III*. Hart et al. (52) found that the Psychopathy Checklist measure was predictive of recidivism in paroled prisoners but that the *DSM-III* diagnosis of antisocial personality disorder had little predictive validity. If the reliability, stability, and predictive validity of the Psychopathy Checklist could be demonstrated in nonprison populations, use of the Psychopathy Checklist could potentially help to clarify the significance of the complex of antisocial and psychopathic behaviors with regard to treatment response in substance abusers.

## CONCLUSIONS

A review of the literature suggests that the relationship between antisocial personality disorder and substance abuse is not yet fully understood. This problem may be magnified by the emphasis in *DSM-III* and *DSM-III-R* on behavioral criteria and their failure to require that antisocial behaviors develop independently of substance abuse. There also may be considerable heterogeneity among substance-abusing patients with antisocial personality disorder with regard to the presence of psychopathic personality features. The absence of these features may be related to the presence of psychoneurotic symptoms and a more favorable treatment response. That is, although the substance abuser with antisocial personality disorder is typically viewed as having a poorer prognosis than other substance abusers, the *DSM-III* and *DSM-III-R* diagnosis of antisocial personality disorder may encompass, at the simplest level of formulation, at least two subgroups—idiopathic and symptomatic psychopaths—who may differ in their ability to experience depression or anxiety and in their ability to form meaningful interpersonal relationships. These factors, in turn, may be related to differential treatment responses. If diagnosis is to be related to prognosis, research on heterogeneity within the population of individuals who manifest antisocial behaviors is crucial.

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# The Temporal Relationship Between Depressive and Psychotic Symptoms in Recent-Onset Schizophrenia

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*The authors examined the temporal relationship between onset of depressive and psychotic symptoms in 27 patients with recent-onset schizophrenia or schizoaffective disorder. Ratings on the Brief Psychiatric Rating Scale were collected every 2 weeks for at least 1 year to specify onset of relapse or exacerbation. Six time periods were defined in relation to onset of psychotic symptoms, and the number of depressive periods was determined for each time period. Onset of depressive periods was concurrent with onset of psychosis more often than expected but was not associated with any other time period. The authors found no distinctive postpsychotic pattern of onset for depression.*

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Although there is general agreement that depression is a serious problem for many schizophrenic patients, the nature and course of depression in schizophrenia remain vague. Several types of depression in schizophrenia have been suggested, including a drug-induced akinesia syndrome (1), schizophrenia-related depression associated with chronic asocial behavior (2), a reactive postpsychotic depression (3), and a residual schizophrenic defect state or "aphanisis" (4). Some authors have argued that "postpsychotic" depression actually begins at the same time psychosis begins but that the depressive symptoms are not noticeable until the florid psychotic symptoms remit (5, 6). Herz and Melville (7) demonstrated that depression is common in the period before onset of psychosis, suggesting that prepsychotic or prodromal depression may be an additional relevant category.

One method of studying these various types of depressive syndromes is to consider the temporal relationship of depressive and psychotic symptoms (5). If depression in schizophrenia is related to periods of psychosis, we might expect to see a systematic relationship between the onset of depression and the onset of psychosis. Prospective ratings of depressive and psychotic symptoms across multiple episodes would allow us to determine if the onset of depression occurred more often during the time periods just before (prodromal), during (concurrent), or after (postpsychotic) the onset of a psychotic episode. Alternatively, the onset of depressive symptoms might be unrelated to the onset of a psychotic episode.

In the present study we looked at the course of symptom ratings from a longitudinal study of patients with recent-onset schizophrenia. Prospective ratings were made every 2 weeks for a period of at least 1 year. The data were treated as categorical variables. We studied the temporal relationship of clinically meaningful psychotic and depressive episodes to clarify empirically whether a pattern of prodromal, concurrent, or postpsychotic depression could be demonstrated in the early phase of schizophrenia.

## METHOD

### *Subjects*

Subjects for the current study were participants in a longitudinal study of the early phase of schizophrenia, Developmental Processes in Schizophrenic Disorders, that examined the nature and determinants of course of illness. Subjects who participated in the current study 1) met Research Diagnostic Criteria (RDC) for schizophrenia or schizoaffective disorder, depressed type, mainly schizophrenic, 2) had had their first psychotic episode within 2 years of intake evaluation, 3) were 18 to 45 years of age, and 4) were Anglo-American or acculturated Hispanic or Asian. All diagnoses were based on an expanded version of the Present State Examination, and all interviewers were trained to a minimum agreement of 85% for the presence of a

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symptom according to the criterion ratings of the Diagnosis and Psychopathology Unit of the Clinical Research Center for the Study of Schizophrenia at the University of California, Los Angeles (Robert P. Liberman, principal investigator). Subjects were excluded for habitual drug or alcohol abuse, evidence of a CNS disorder, or mental retardation.

For the purpose of the current study, we selected only those subjects (N=27) who showed any features of both depressive and psychotic symptoms during the follow-up period. Twenty-two of these subjects met criteria for schizophrenia, and five met criteria for schizoaffective disorder, depressed type, mainly schizophrenic. All subjects provided informed consent to participation in the study.

### *Symptom Ratings*

Symptom ratings were made on an expanded version of the Brief Psychiatric Rating Scale (BPRS) (8) that includes behavioral anchors (9). The ratings were made every 2 weeks by clinicians who were trained to a reliability criterion (median intraclass correlation across items) of at least 0.80. Three BPRS scales were used to rate psychotic symptoms: unusual thought content, hallucinations, and conceptual disorganization. The three BPRS scales used to rate the depressive symptoms were depression, guilt, and suicidality. Factor analyses of the BPRS have shown the depressive symptoms to be independent of the psychotic symptoms (10).

### *Relapse Criteria*

We used previously developed BPRS criteria (unpublished paper of K. Nuechterlein et al.) for a relapse or a significant exacerbation that defined the onset of a psychotic episode.

A psychotic relapse involved a severe—6—or very severe—7—rating on any one of the three psychotic scales after a remission lasting for at least 1 month. Remission was defined as a period of at least 1 month when the patient maintained a score of 3 or less on all psychotic scales.

Significant psychotic exacerbation involved a moderately severe—5—rating on any of the psychotic scales plus an increase of at least 2 points on one of the other psychotic scales after a remission lasting at least 1 month. Significant psychotic exacerbation was also rated if the subject scored 5 on one of the psychotic scales for more than 1 month following remission.

Significant psychotic exacerbation following persisting psychotic symptoms was rated when the subject continued to have a score of 4 or more on one of the psychotic scales and then showed at least a 2-point increase to a 6 or 7 or showed a 1-point increase in this scale (to a 6 or 7) and an accompanying 2-point increase on another psychotic scale. This category was included because we were primarily interested in relapse or exacerbation of psychotic symptoms, even when full remission was not obtained.

Following the previously developed BPRS criteria (unpublished paper of K. Nuechterlein et al.), we defined the onset of a depressive episode in a way that paralleled the definition of the onset of a psychotic episode. The only difference was the inclusion of the category of mild depressive exacerbation to allow for the detection of low levels of depressive symptoms.

Depressive relapse involved a severe—6—or very severe—7—rating on any of the three depressive scales after a remission lasting at least 1 month (scores of 3 or below on all three depression scales).

Significant depressive exacerbation involved a moderately severe—5—rating on any depressive scale plus an increase of 2 points on another of the scales following at least 1 month of remission. Significant depressive exacerbation was also rated if the patient scored 5 on one of the depressive scales for more than 1 month following remission.

Significant depressive exacerbation following persisting depressive symptoms was rated when the patient continued to have a score of 4 or above on one of the depressive scales and then showed a 2-point increase to a score of 6 or 7, or showed a 1-point increase on this scale (to a 6 or 7) and an accompanying 2-point increase on another depressive scale.

Mild depressive exacerbation was rated when a moderate—4—rating was obtained on one of the depressive scales for at least 1 month following remission.

### *Time Periods*

Six discrete time periods were defined that used the onset of a psychotic episode as a reference point: 1) prodromal—the 8-week period before the onset of a psychotic episode, 2) concurrent—the 2-week period during which the psychotic symptoms reached BPRS criteria for a psychotic episode, 3) soon after psychotic onset—the first 4 weeks after onset of psychosis, 4) long after psychotic onset—the period from the end of the first 4 weeks after psychotic onset until the patient entered psychotic remission, 5) postpsychotic—the 8-week period after the end of a psychotic episode, and 6) "other"—any remaining periods during which the BPRS ratings were obtained.

## RESULTS

The patients were followed for a mean of 153 weeks (range=57–297 weeks). Figure 1 shows the proportion of time spent in each of the six time periods by the 27 patients. Patients spent 54.8% of their time in a nonpsychotic period that was not near a psychotic episode and 23.6% of their time in a sustained psychotic period more than 1 month after onset of the psychotic episode. The remaining time was divided among the other four categories: 7.4% for prodromal, 3.0% for concurrent, 4.2% for soon after, and 7.0% for

**FIGURE 1. Phases of Psychotic Episodes Experienced by 27 Patients With Recent-Onset Schizophrenia or Schizoaffective Disorder**

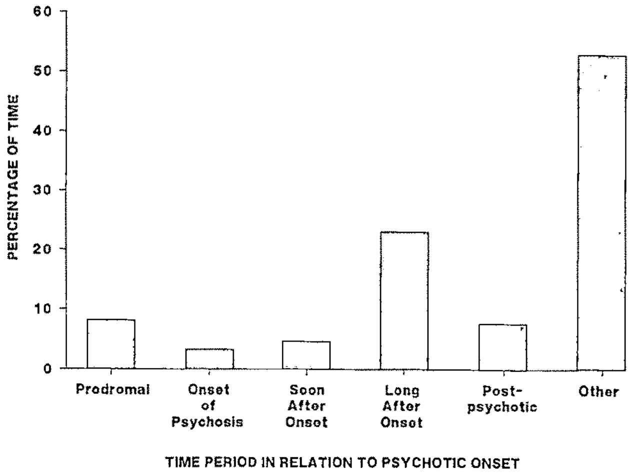
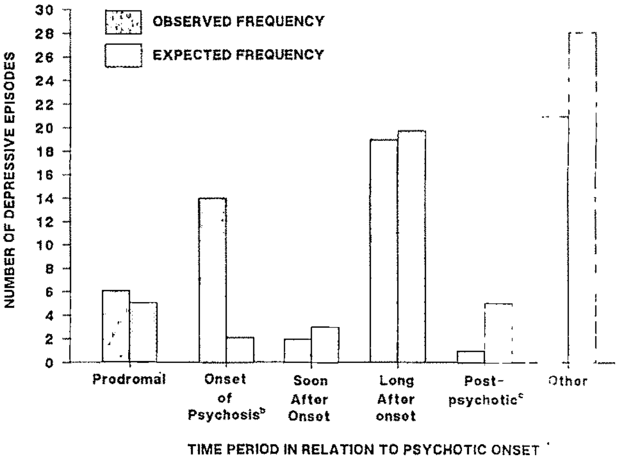


**FIGURE 2. Onset of Depression During Phases of Psychotic Episodes of 27 Patients With Recent-Onset Schizophrenia or Schizoaffective Disorder**



[a] $\chi^2=72.83$, df=5, $p<0.00001$.
[b] $\chi^2=67.2$, df=1, $p<0.0001$.
[c] $p<0.07$.

postpsychotic. Only six of the patients failed to achieve full remission after a psychotic episode during the follow-up period.

A total of 63 depressive onsets were observed over the six time periods, with a mean±SD number of 2.33±1.27 depressive periods per patient. Eighteen of the 27 patients had more than one depressive episode during the follow-up period. Of these 18 patients, only three had all of their depressive episodes within one type of time period. Two of these patients had all of their episodes in the "long after" period, and one had the episodes in the "other" period.

We determined an expected frequency of depressive episodes for each patient for each of the time periods on the basis of the relative duration of the time periods. These expected frequencies were then summed across patients to yield an overall expected frequency for each time period. Figure 2 compares the expected frequencies of the depressive onsets to the observed frequencies. As seen in figure 2, the difference in the distributions was highly significant.

The onset of depression was concurrent with the onset of psychosis to a highly disproportionate degree (see figure 2). Although two depressive onsets would be expected during this period, 14 were found. The postpsychotic period showed a nonsignificant tendency to have too few depressive episodes (see figure 2). The six patients who did not experience full remission following psychotic relapse did not contribute to the observed or expected frequencies for this period. Therefore, the results for the postpsychotic period would be the same even if these patients were excluded. The remaining categories did not differ from the expected frequencies.

The same analyses were conducted after excluding the five patients with schizoaffective disorder. The chi-square values increased following the exclusion (92.3 for the overall value, 87.8 for the concurrent period). Therefore, the present results are not attributable to the inclusion of the schizoaffective patients.

## DISCUSSION

These categorical analyses indicate that the simultaneous appearance of pathological levels of depressive and psychotic symptoms during the early phase of schizophrenia occurs much more frequently than expected by chance. Onset of depressive symptoms showed a nonsignificant tendency to occur less often than expected by chance during the 8-week period following the end of a psychotic episode. No evidence for an increased frequency of onset during the ongoing psychotic periods was found. Thus, at least during this early phase of schizophrenia, no evidence for a class of discrete postpsychotic depressive onsets was present. Furthermore, the onset of depressive symptoms during the prodromal period of psychotic episodes was not significantly more frequent than expected by chance.

The current results appear to run counter to the concept of a specific postpsychotic depression in schizophrenia. Depression occurred during the postpsychotic period, but at a frequency that was less than the expected frequency. Our results are more consistent with the notion that depression begins at the same time as psychosis but may not be clinically prominent until psychotic symptoms subside (5).

A recent study by Subotnik and Nuechterlein (11) drew subjects from the same longitudinal project and compared each subject's BPRS scores from two time periods: one that preceded a psychotic relapse and one that did not. They found that depression and guilt scale scores were higher during the prodromal period than in the control period. This finding might appear inconsistent with the present results because we did not find more depressive episodes during the prodromal period than in other periods. However, a number of methodological differences could account for the apparent discrepancy. First, the Subotnik and Nuechterlein study compared the prodromal period with a period unrelated to psychosis, but in the present study we compared observed frequency to expected frequency for a given time period. Thus, we did not compare the prodromal period (where we found a slight excess of depressive onsets) directly with the "other" period (where we found a relative reduction of onsets). Second, only psychotic relapse, not the two categories of psychotic exacerbation, was considered in the earlier study. Use of the psychotic exacerbation categories in addition to the psychotic relapse category may move the prodromal period to a somewhat earlier point. Third, the sample selection differed in that, unlike the earlier study, the present study excluded patients without a depressive period. Finally and most importantly, the previous study rated depressive level, but the present paper considered the time of depressive onset. The focus of the current paper was the temporal relationship of psychotic and depressive onsets, not the average severity of depression during any given period. Given the differences in selection criteria and emphasis, we would not necessarily expect similar results.

In summary, our data support the notion that depressive onset occurs concurrent with psychotic onset to a disproportionate degree. Although depression also occurs in the periods before or after the psychotic episodes, it does not appear more often than expected by chance. One possible limitation of the present study is that the data were treated only in a categorical fashion. Such an approach carries clinical significance because it reduces the data to noteworthy levels of psychotic and depressive symptoms, which are usually the focus of treatment programs. A disadvantage of this analysis is that it focused only on the onset of symptoms, not the offset. In addition, depressive scores were ignored if they did not reach a threshold of clinical significance. Therefore, the relationship between psychotic symptoms and subclinical changes in depression (e.g., within the mild range) remains unknown. We are currently trying to apply time series analyses to the data in order to address these methodological issues.

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# Marital Therapy: A Viable Treatment for Depression and Marital Discord

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*Thirty-six maritally discordant couples with depressed wives were randomly assigned to marital therapy, cognitive therapy, or a waiting-list control condition. The women given marital or cognitive therapy showed significant and clinically meaningful reductions in their depression. The women given marital therapy showed greater increases in marital satisfaction than did those given cognitive therapy or no therapy; these differences were maintained at 1-year follow-up. These findings suggest that marital therapy may be the most effective and appropriate treatment for clinically significant marital discord with coexisting clinically significant depression.*

(Am J Psychiatry 1990; 147:183–186)

Marital discord is the most common life stressor that is a precursor to depression (1). Relapses of depression following acute depressive episodes and following pharmacological treatment of depression are often precipitated by marital disruption (2, 3). Given the association between depression and marital discord, and given the fact that in more than 50% of maritally discordant couples at least one spouse is depressed (4), we compared two well-developed treatments—behavioral marital therapy (5, 6) and cognitive behavioral therapy (7–9)—in the treatment of such couples.

In a pilot study with eight women who were depressed and whose marriages were discordant, behavioral marital therapy led to a reduction in both depression and marital discord, whereas cognitive therapy for the women was associated only with a significant reduction in depression (10). The present study provides a more complete comparison of the clinical efficacy of behavioral marital therapy and cognitive therapy in reducing depression and increasing marital satisfaction.

Behavioral marital therapy for depression places emphasis on increasing feelings of closeness, open sharing of thoughts and concerns, positive interchanges, and effective problem-solving strategies for resolving marital disputes. Cognitive behavioral therapy places emphasis on increasing positive beliefs about the self, the world, and the future and on decreasing negative cognitive distortions and selective memories for negative events.

## METHOD

As part of an ongoing treatment outcome study, 36 couples were randomly assigned to individual cognitive therapy for the depressed wife (N=12), conjoint marital therapy for the depressed wife and her spouse (12 couples), or a 15-week waiting list (12 couples). Subjects were recruited by means of announcements in newspapers for a depression–marital therapy treatment program.

All subjects provided informed consent to participation in the study after its nature had been explained to them.

Both behavioral marital therapy and cognitive therapy lasted for 15–16 weeks. The couples in behavioral marital therapy and the women in cognitive therapy were seen on a weekly basis. The therapy protocol allowed for up to 2 hours of emergency phone consultation for the 16 weeks if such help were needed.

To be included in the study, the women had to meet *DSM-III* diagnostic criteria for major depression or dysthymic disorder. Ten women in individual cognitive therapy, 11 women in marital therapy, and 11 women in the waiting-list control group were diagnosed as having major depression, single episode. Two women in individual therapy, one woman in marital therapy, and one woman in the control group did not meet criteria for major depression and were diagnosed as having dysthymic disorder. All of the women were interviewed with the Structured Clinical Interview for DSM-III (SCID) (11), a standard diagnostic interview. Approximately half of the women in each of the three groups received a second diagnosis in addition to de-

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pression. The women had to have a Beck Depression Inventory score of 14 or more (12, 13). Women who were actively suicidal were not included in the main portion of this study because they could not be randomly assigned to the waiting-list control condition (unpublished 1987 paper of K.D. O'Leary et al.).

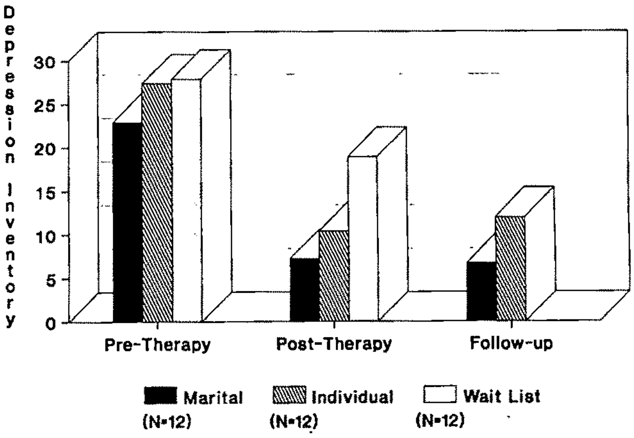
One or both partners in the marriage had to have a score of 100 or less (significantly maritally discordant) on the Dyadic Adjustment Scale (14). Subjects also had to describe themselves as maritally discordant or as having substantial marital problems during the marital interview. Three couples in the marital therapy group and three women in the individual therapy group dropped out of treatment before five sessions. Their data are not included here. No subjects were receiving medication for depression.

The average age of the women was 39.3 years (range=28–59). The average number of children per family was 2.5 (range=0–7), and the average educational level of the women was 13.9 years (range=9–21). Three therapists provided both cognitive therapy and marital therapy. Two of the therapists were doctoral level psychologists and one was a fifth-year graduate student in clinical psychology. All therapists had at least 4 years of full-time graduate training in clinical psychology in a program nationally recognized for training in behavior therapy. All therapists had participated in a one-semester behavioral marital therapy seminar and an associated year-long practicum. They had also participated in a year-long intervention course and associated year-long practicum emphasizing cognitive behavior therapy. In preparation for this clinical research, the therapists were trained for 30 hours in each of the two treatments by nationally recognized experts before seeing patients (cognitive therapy: Dr. Craighead, Duke University, and Dr. Epstein, University of Maryland; marital therapy: Dr. Baucom, University of North Carolina, and Dr. O'Leary, State University of New York, Stony Brook). Before any of the patients were seen, the therapists had to be judged by the experts as competent service providers of the two therapies. In addition, the recognized experts provided periodic clinical supervision to the therapists.

## RESULTS

Both behavioral marital therapy and cognitive individual therapy were effective in reducing depressive symptoms in the women given these therapies (figure

**FIGURE 1. Changes in Depression Scores in Women Given Marital Therapy or Individual Cognitive Therapy and Women in a Waiting-List Control Group**



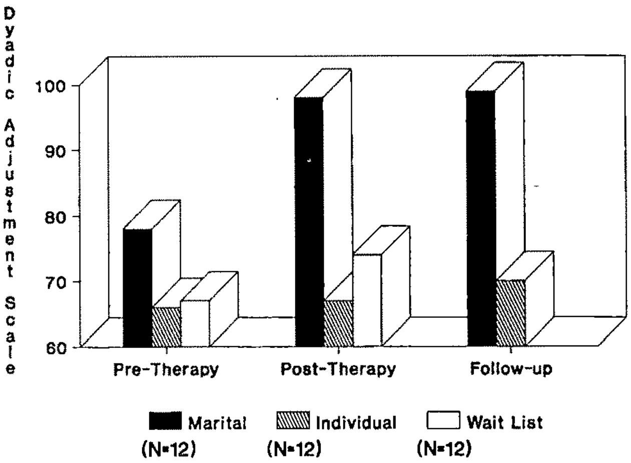
the individual therapy group (F=5.23, df=1, 21, p=0.032) had significantly lower depression scores than the women in the waiting-list control group. The depression scores of the women in marital therapy and in individual therapy did not differ significantly from each other after therapy (F=1.23, df=1, 22, p=0.278).

Analyses of variance (ANOVAs) indicated that there were significant differences in marital satisfaction across the three groups after treatment (F=5.13, df=2, 33, p=0.012). The women given marital therapy had significantly higher marital satisfaction scores after therapy than did the women given cognitive therapy (F=8.65, df=1, 22, p=0.008) and the women in the waiting-list control group (F=7.65, df=1, 22, p=0.011). However, the marital satisfaction scores of the women in individual therapy did not differ from those of the women in the waiting-list control group (F=0.42, df=1, 22, p=0.526).

Despite some numerical differences on the Dyadic Adjustment Scale and the Beck Depression Inventory, the three groups of women did not differ significantly on these measures before treatment. Furthermore, an analysis of covariance, controlling for pretreatment differences, yielded the same results pre- to posttreatment for both the Dyadic Adjustment Scale and the Beck Depression Inventory.

ANOVAs indicated that the women given marital therapy did not have lower depression scores at follow-up than the women given cognitive therapy

**FIGURE 2. Changes in Marital Satisfaction Scores in Women Given Marital Therapy or Individual Cognitive Therapy and Women in a Waiting-List Control Group**



marital therapy). However, in the absence of treatment, there was a significant association between Beck Depression Inventory scores before and after treatment ($r=0.52$, $N=12$, $p<0.05$). Conversely, pretreatment marital satisfaction scores were very highly related to marital satisfaction scores after treatment for all groups ($r=0.72$, $N=12$, $p<0.01$ for behavioral marital therapy, $r=0.80$, $N=12$, $p<0.01$ for cognitive therapy, and $r=0.92$, $N=12$, $p<0.01$ for the waiting-list control condition). This association was especially consequential in cognitive therapy: on average, women with the lowest initial marital satisfaction scores showed a deterioration in level of marital satisfaction over the course of cognitive therapy. Women in marital therapy who had had the lowest initial marital satisfaction scores made gains comparable to those with higher initial marital satisfaction scores.

Since there were only three treated women who did not meet criteria for major depression, it was not possible to evaluate statistically whether these women fared differently than the subjects with a diagnosis of major depression.

## DISCUSSION

These results clearly demonstrate the utility of marital therapy for depression. Marital therapy and cognitive individual therapy were associated with clinically significant reductions in depression. The women given marital therapy evidenced as much change in depression as did the women given cognitive behavior therapy, a finding that we believe reflects the impact that marital satisfaction can have on depression. The marital therapy did not focus directly on changes in cognitive distortions or in beliefs about self, the world, and the future. Thus, it appears that marital therapy changed the levels of depression in these women by increasing their marital satisfaction.

The correlations of Beck Depression Inventory scores before and after treatment showed that the initial level of severity of depression was not significantly related to outcome in this sample of mild to moderately depressed women. However, level of initial severity of marital discord was very highly related to outcome: only those women who received marital therapy showed consistent patterns of improved marital satisfaction. We cannot expect marital satisfaction to improve with cognitive therapy in depressed women experiencing marital discord. On the other hand, we can expect depression to improve with either behavioral marital therapy or cognitive therapy in depressed women experiencing marital discord. Furthermore, initial levels of depression were not significantly related with levels of depression after treatment for either group.

Marital dissatisfaction is often harder to change than depression. Changes in two individuals rather than one are necessary. If both partners are not motivated to change, then aiming for improvement in marital satisfaction may not be the best goal for therapy. Sometimes, separation and/or divorce may be legitimate and desirable goals. In these cases, individually focused treatments would clearly be preferable. In addition, not all depressed patients report substantial marital discord. Marital therapy should not be considered the treatment of choice for these patients. All couples included in the present study, however, expressed a desire to improve their relationships, and there was no differential rate of separation or divorce across the two treated groups. Overall, these results demonstrate the importance of assessing marital discord in women presenting with symptoms of mild to moderate depression before recommending a particular treatment.

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# Subcortical Hyperintensity on Magnetic Resonance Imaging: A Comparison of Normal and Depressed Elderly Subjects

C. Edward Coffey, M.D., Gary S. Figiel, M.D., William T. Djang, M.D.,
and Richard D. Weiner, M.D., Ph.D.

*Subcortical hyperintensity on $T_2$-weighted brain magnetic resonance imaging was significantly more common and more severe in elderly depressed patients referred for ECT than in a matched control group of normal elderly subjects. The potential clinical and research implications of these findings are discussed.*

(Am J Psychiatry 1990; 147:187–189)

We have previously reported (1–4) that elderly depressed patients referred for ECT frequently exhibit changes (foci of signal hyperintensity) in the subcortical white matter and gray matter nuclei on $T_2$-weighted brain magnetic resonance imaging (MRI). These findings are of interest given the well-known association between affective disturbances and syndromes associated with subcortical brain disease (Huntington's chorea, multiple sclerosis, etc.). The significance of subcortical hyperintensity in patients with depression remains unclear, however, since similar changes have also been noted on the MRI scans of apparently normal elderly individuals who have no active neurologic disease (see reference 4 for a review). To address this issue we compared the prevalence and severity of subcortical hyperintensity observed in our elderly depressed patients to that of an age- and sex-matched control group with no history of neurologic or psychiatric illness.

## METHOD

The subjects were 51 elderly (60 years of age or older) inpatients, all right-handed, who received brain MRI prior to a course of ECT for severe major depression (diagnosed according to a *DSM-III* checklist administered by the ECT service). Sixteen of these depressed patients also had histories of neurologic illness (e.g., mild dementia, stroke, Parkinson's disease), but none met the *DSM-III* criteria for an organic affective disorder. Additional clinical details on this group and the results of their MRI scans have been previously described (3). The control group consisted of a new sample of 22 age- and sex-matched elderly volunteers, all right-handed, recruited from the community. Each control subject received a structured medical and neuropsychiatric history interview and examination by a research psychiatrist (G.S.F.); none had a history of any neurologic or psychiatric illness, and all denied any use of psychotropic medications.

The brain MRI studies were performed on a General Electronics 1.5-tesla Signa system. Spin-echo pulse sequences were used to generate a series of 15 $T_2$-weighted images (repetition time=2500 msec, echo times=40 and 80 msec) in the axial plane. Sections were 5 mm thick, with a 2.5-mm interscan gap; additional technical parameters included a 128×256 matrix, a 20-cm field of view, and two excitations.

The brain MRI scans were coded and randomized and then analyzed independently by a Board-certified neuroradiologist (W.T.D.) and a neurologist/psychiatrist (C.E.C.), both of whom were blind to the subject groups (depressed and control). Using formal ratings of subcortical hyperintensity (4, 5), these investigators assessed each subject's MRI study for the presence and extent of the following findings:

1. *Periventricular hyperintensity*, graded as 0=absent, 1="caps," or pencil-thin lining, 2=smooth "halo," and 3=irregular periventricular hyperintensity extending into the deep white matter.
2. *Deep white matter hyperintensity*, separate foci of hyperintensity in the deep white matter rated as 0=absent, 1=punctate foci, 2=beginning confluence of foci, and 3=large confluent areas. Predefined visual standards for each grade of periventricular and deep white matter hyperintensity were established for comparison (see reference 5 for examples).
3. *Changes in the subcortical gray matter nuclei* (basal ganglia, thalamus), abnormalities rated as either punctate, multipunctate, or diffuse; any left-right asymmetries were noted.

The initial subcortical hyperintensity scores differed

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**TABLE 1. Clinical and Brain MRI Findings in Elderly Normal Control Subjects and in Elderly Inpatients With Major Depression**

| | | | Depressed Inpatients | | | | | |
|---|---|---|---|---|---|---|---|---|
| | Normal Control Subjects (N=22)[a] | | Without Neurologic History (N=35)[b] | | With Neurologic History (N=16)[c] | | Total (N=51) | |
| Item | N | % | N | % | N | % | N | % |
| Vascular risk factors | | | | | | | | |
| Male sex | 7 | 32 | 7 | 20 | 8 | 50 | 15 | 29 |
| Hypertension | 3 | 14 | 8 | 23 | 6 | 38 | 14 | 27 |
| Diabetes mellitus | 1 | 5 | 0 | 0 | 1 | 6 | 1 | 2 |
| Coronary artery disease | 7 | 32 | 5 | 14 | 3 | 19 | 8 | 16 |
| Stroke | 0 | 0 | 0 | 0 | 7 | 44 | 7 | 14 |
| Periventricular hyperintensity | | | | | | | | |
| Grade 1 | 17 | 77 | 15 | 43 | 4 | 25 | 19 | 37 |
| Grade 2 | 5 | 23 | 15 | 43 | 4 | 25 | 19 | 37 |
| Grade 3 | 0 | 0 | 5 | 14 | 8 | 50 | 13 | 25 |
| Deep white matter hyperintensity | | | | | | | | |
| None | 5 | 23 | 6 | 17 | 1 | 6 | 7 | 14 |
| Grade 1 | 14 | 64 | 13 | 37 | 3 | 19 | 16 | 31 |
| Grade 2 | 3 | 14 | 10 | 29 | 6 | 38 | 16 | 31 |
| Grade 3 | 0 | 0 | 6 | 17 | 6 | 38 | 12 | 24 |
| Lesions of deep gray nuclei (thalamus/basal ganglia) | 1 | 5 | 14 | 40 | 12 | 75 | 26 | 51 |

[a] Mean±SD age=70.7±5.5 years.
[b] Mean±SD age=71.7±8.1 years.
[c] Mean±SD age=71.7±6.8 years.

between the two raters for only five (7%) of the 73 subjects, and the differences were never greater than one rating level, indicating a high degree of interrater agreement. In cases where disagreement occurred, the MRI scans were reanalyzed, and a consensus rating of the abnormality was established by the two raters.

On the basis of the reported occurrence and severity of subcortical hyperintensity in normal elderly subjects (4–7), we hypothesized that grade 2 and grade 3 periventricular and deep white matter hyperintensity would be more common in our depressed inpatients than in the control group. We also hypothesized that lesions of the subcortical gray nuclei would be more common in the depressed patients than in the normal control subjects. The frequency of these MRI changes was compared using 2×2 tables, and statistical significance was evaluated using the chi-square test. In cases where the chi-square test was inappropriate due to insufficient cell sizes, Fisher's exact test was used.

## RESULTS

Predominantly mild changes of subcortical hyperintensity were observed in all of the normal control subjects (see table 1). Periventricular caps were seen in 17 of the normal control subjects; the remaining five subjects exhibited a more or less smooth halo (grade 2) of periventricular hyperintensity. Separate foci of $T_2$ hyperintensity in the deep white matter were also seen in 17 of the normal subjects. These changes appeared either as punctate foci (grade 1) or as areas of small confluence (grade 2). No normal subject exhibited severe (grade 3) periventricular or deep white matter hyperintensity. Foci of $T_2$ hyperintensity in the subcortical gray nuclei were observed in only one of the normal control subjects.

Subcortical hyperintensity was also present in all of the depressed subjects, but the changes were more severe than in the control group (table 1). Comparing only the depressed subjects without any history of neurologic illness and the control group, we found that moderate and severe periventricular hyperintensities were significantly more common in the depressed group than in the control group ($\chi^2=4.9$, df=1, p=0.03), as were moderate and severe deep white matter hyperintensities ($\chi^2=5.18$, df=1, p=0.02). Similarly, lesions of the thalamus/basal ganglia were significantly more common in the depressed patients than in the normal control group (Fisher's exact test, p=0.003).

For both the control and the depressed groups, the severity of subcortical hyperintensity appeared to be related to the presence of risk factors for vascular disease. Among the control subjects, for example, moderate periventricular hyperintensity appeared to be more common in subjects with (four of 14, 29%) than in those without (one of 8, 13%) vascular disease, and every control subject with either moderate deep white matter hyperintensity (N=3) or lesions of the deep gray nuclei (N=1) had vascular disease. Similarly, depressed subjects with histories of neurologic illness had the highest prevalence rates of moderate and severe subcortical hyperintensities (table 1), and even among the 35 subjects with no neurologic history, the 13 with vascular risk factors tended to have higher rates of moderate and severe deep white matter hyperintensities (54%) and lesions of the deep gray nuclei (54%) than the 22 without vascular disease (41% and 32%, respectively).

## DISCUSSION

There are two major findings from this study. First, while subcortical hyperintensity on MRI was common in the normal elderly subjects, the white matter changes typically were neither severe nor extensive, and lesions of the subcortical gray nuclei were decidedly rare. This observation is in close agreement with previous studies that have examined the occurrence and severity of subcortical hyperintensity in small numbers of normal subjects (4–7). A second finding from our study is that in the elderly depressed patients referred for ECT, white matter hyperintensity was significantly more severe and lesions of the subcortical gray nuclei were significantly more common than in the normal control group with similar age and prevalence of vascular disease.

Our results have several implications for the research methods used in MRI studies of subcortical hyperintensity. First, the findings highlight the critical importance of appropriate control groups; for example, since the severity of subcortical hyperintensity is related in part to vascular disease, it is imperative that this variable be controlled whenever comparisons among groups are made. The potential impact of other factors (smoking, hypercholesterolemia, etc.) may also need to be considered. Second, psychiatric patients (at least those who are depressed) are not valid control subjects for studies of subcortical hyperintensity; even among our depressed patients with no history or clinical evidence of neurologic illness, subcortical hyperintensity was more severe than it was in the normal control group. Finally, our results demonstrate the importance of using formal rating scales to assess the severity and extent of subcortical hyperintensity. For example, no differences between our elderly depressed and control subjects would have been revealed if the comparisons had been based solely on the neuroradiologist's clinical report of the presence or absence of foci of subcortical hyperintensity.

Our findings point to the need for additional research. First, it is important to determine the prevalence and severity of subcortical hyperintensity in nonelderly depressed patients as well as in patients with other psychiatric disorders (schizophrenia, anxiety disorders, etc.). In this regard, Dupont et al. (8) found that white matter hyperintensity was more common in young patients with bipolar disorder (N=14) than in age-matched control subjects (N=8). The relative prevalence of vascular disease in the two groups was not described, however, and severity ratings of subcortical hyperintensity were not provided. Second, we need to identify factors that may be related to the prevalence of subcortical hyperintensity in depressed patients; malnutrition, weight loss, drug and alcohol use, neglect of physical health, and poor compliance with regimens of medications (including antihypertensive drugs) might all be contributing factors. Subcortical hyperintensity might also be related to therapy for depressive illness. Although we have found that prior ECT is not associated with subcortical hyperintensity (2, 3), antidepressant medications, with their known hypotensive effects, could conceivably cause repeated episodes of subclinical cerebral ischemia that might contribute to the development of this condition. Third, we need to evaluate the potential impact of subcortical hyperintensity and related brain changes on the clinical phenomenology, response to treatment, and course of illness in patients with affective disorders. Finally, the potential relationship between subcortical hyperintensity and the pathophysiology of depressive illness demands further investigation. As we have discussed, affective disturbances are common in syndromes associated with subcortical brain disease, and at least some patients with depression have been found to exhibit anatomic and functional changes in subcortical brain regions, including ventriculomegaly (9) and reduced metabolism of the caudate nuclei (10). Further study is underway in our laboratory to investigate whether subcortical hyperintensity and related structural brain changes are actually associated with neurobiologic and functional alterations that may mediate affective illness.

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# Relationship Between Hopelessness and Ultimate Suicide: A Replication With Psychiatric Outpatients

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*A prospective study of 1,958 outpatients found that hopelessness, as measured by the Beck Hopelessness Scale, was significantly related to eventual suicide. A scale cutoff score of 9 or above identified 16 (94.2%) of the 17 patients who eventually committed suicide, thus replicating a previous study with hospitalized patients. The high-risk group identified by this cutoff score was 11 times more likely to commit suicide than the rest of the outpatients. The Beck Hopelessness Scale thus may be used as a sensitive indicator of suicide potential.*

(Am J Psychiatry 1990; 147:190–195)

Suicide is the ninth leading cause of death in the United States, occurring with a ratio of approximately 11 deaths per 100,000 population (1). Over the last few decades, researchers have been pursuing the challenge of identifying persons at high risk for suicide by studying epidemiological, behavioral, and psychological variables.

Negative expectation or hopelessness is among the psychological variables that have shown promise in the prediction of suicide. Beck (2) studied 50 depressed suicidal patients who had undergone long-term psychotherapy and perceived the common theme of hopelessness underlying their suicidal wishes. He noted that "The suicidal preoccupations . . . seem related to the patient's conceptualization of his situation as untenable or hopeless" (pp. 327–328). This sense of hopelessness led the suicidal patients to believe that suicide was the only feasible strategy for dealing with their seemingly insoluble problems.

According to Beck (3), the critical role that hopelessness plays in suicide is illustrated in the sequence of events that leads a depressed individual to commit suicide. The patient systematically misconstrues his or her experience in a negative way and anticipates dire outcomes for his or her problems. Ultimately, the patient is drawn to the idea of suicide as a way out of his or her "insoluble problems."

The central role of hopelessness in the development of suicidal ideation has been supported by empirical research (4–7). Wetzel et al. (8) reviewed studies addressing the relationships among depression, hopelessness, and suicidal ideation and concluded that the preponderant evidence supported the linkage of hopelessness and suicide intent. In a 10-year prospective follow-up study of 165 patients hospitalized with suicidal ideation, Beck et al. (9) reported that hopelessness was predictive of actual suicide. Of the 11 patients who eventually committed suicide, 10 (90.9%) had Beck Hopelessness Scale (10) scores of 9 or greater. Only one patient (9.1%) who eventually committed suicide had a score lower than 9. The mean Beck hopelessness score was significantly higher in the patients who committed suicide (mean±SD=13.27±4.43) than in the patients who did not (mean±SD=8.94±6.05) ($t=2.33$, $df=163$, $p<0.05$). Furthermore, length of follow-up was not related to detecting more eventual suicides.

The present study is an extension of the investigation of Beck et al. (9) to an outpatient population. Specifically, we sought to ascertain whether level of hopelessness measured during an index evaluation at an outpatient clinic would predict eventual suicide in psychiatric outpatients, as it did in a hospitalized sample.

## METHOD

### Sample

The sample consisted of the 1,958 consecutive outpatients evaluated at the Center for Cognitive Therapy between September 1978 and February 1985 who completed both the Beck Hopelessness Scale and the Beck Depression Inventory (11). Patients were either

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self-referred or referred by other professionals. There were 1,135 (58.0%) women and 823 (42.0%) men. The mean±SD age of the sample was 36.12±12.39 years (range=15–84 years). According to *DSM-II* and *DSM-III* criteria, approximately 40% had affective disorders, 15% had anxiety disorders, 25% had a combination of depression and anxiety disorders, and the remaining 20% had miscellaneous other disorders (e.g., substance abuse, marital problem, adjustment disorder, schizophrenia).

### *Procedure*

Following telephone contact with intake personnel at the center, each patient was scheduled for a complete clinical evaluation, which usually took place within 1 week. In addition to a 2-hour interview with a trained clinician, each patient spent 1 hour completing a battery of self-report tests, including the Beck depression and hopelessness scales.

All patients were diagnosed by the interviewing clinician according to either *DSM-II* or *DSM-III*. Each diagnosis was thoroughly reviewed by a senior staff member within the following week to confirm that all relevant criteria were met and that possible exclusionary criteria were considered. The final diagnosis reflected a consensus between the interviewing and consulting clinicians.

Individuals who were considered as possibly suitable for treatment at the center were scheduled for an intake interview with a clinician. Those excluded from intake evaluation and referred elsewhere consisted of individuals who presented clear evidence of an organic disorder, the manic phase of a bipolar disorder with no medication, or a condition requiring immediate hospitalization (e.g., severe suicide risk or psychosis).

The Beck Hopelessness Scale (10) is a 20-item true-false self-report instrument that assesses the degree to which a person holds negative expectations about the future. Nine of the items are keyed false and 11 true. The items are summed to obtain a total hopelessness score (range=0–20). In a sample of 294 hospitalized patients who had made suicide attempts, the Kuder-Richardson reliability (KR21) coefficient for the Beck Hopelessness Scale was 0.93, and all of the item-total correlations, ranging from 0.39 to 0.76, were significant. Moderately high correlations ranging from 0.56 to 0.68 between the Beck Hopelessness Scale and the Beck Depression Inventory have been reported in a number of studies with samples of hospitalized patients who attempted suicide (7) and depressed patients (12).

The Beck Depression Inventory (11) consists of 21 items, each consisting of four statements that reflect gradations in the intensity of a particular depressive symptom. The respondent chooses the statement that best corresponds to the way that he or she has felt for the past week. The individual statements are scored from 0 to 3 and summed to obtain a total depression score (range=0–63). The psychometric properties of the inventory have been reviewed by Beck and Steer (11).

### *Follow-up*

The study was initially limited in scope to patients residing in Philadelphia who terminated treatment at the center in 1982. To ascertain whether any patients in this cohort had committed suicide, death certificates on file at the office of the Philadelphia medical examiner were scanned for matches with the names of patients in the study cohort. When a match was found, information regarding cause of death was recorded verbatim from the certificate. Because there are difficulties with respect to the representativeness of locally obtained medical examiner data (13), the following procedure was also implemented.

To follow up patients residing outside the jurisdiction of the Philadelphia medical examiner and to examine several years at once, we used the National Death Index, a service of the National Center for Health Statistics. This index is a central computerized index of death record information that is compiled from data periodically submitted by individual state vital statistics offices. Identifying information provided by the user is checked against corresponding information in the National Death Index database, which currently covers deaths occurring from 1979 to 1985, and the user is notified whether one of the records supplied matches a database record.

We performed searches covering the years 1979 to 1985. When a likely match was found, arrangements were made with the state vital statistics offices to obtain copies of death certificates. Determinations regarding cause of death were made on the basis of information contained in the death certificates. The records of the National Death Index disclosed the same deaths, causes, and modes of death as those on file in the Philadelphia medical examiner's office.

## RESULTS

### *Follow-up*

Patients were followed up from date of evaluation until December 31, 1985. The mean±SD length of follow-up was 43.00±20.71 months (range=8.20–89.57 months). Of the 1,958 patients who were evaluated (but not necessarily treated) at the clinic, 31 (1.6%) died during the follow-up period. Of these 31 patients, 17 (54.8%) committed suicide and 12 (38.7%) died from natural causes; in two cases (6.5%) the official completing the death certificate could not classify the cause of death as natural, accidental, suicide, or homicide. Cases in this last category were dropped from all further analyses.

At intake, the patients who eventually committed suicide ranged in age from 18 to 59 years (mean±SD=

40.35±11.61). Nine (52.9%) of these patients were men and eight (47.1%) were women. Thirteen received diagnoses of recurrent major depression (or chronic depressive neurosis), three diagnoses of bipolar disorder, and one a diagnosis of adjustment disorder with depressed mood.

Ten (58.8%) of the 17 patients who committed suicide received cognitive therapy, whereas seven (41.2%) were just evaluated for cognitive therapy and did not enter therapy. The number of visits ranged from one to 25. Only one patient (5.9%) was in treatment at the time of his suicide. Eight (47.1%) had made at least one prior suicide attempt, and five (29.4%) had received an alcohol-related diagnosis.

### *Group Differences*

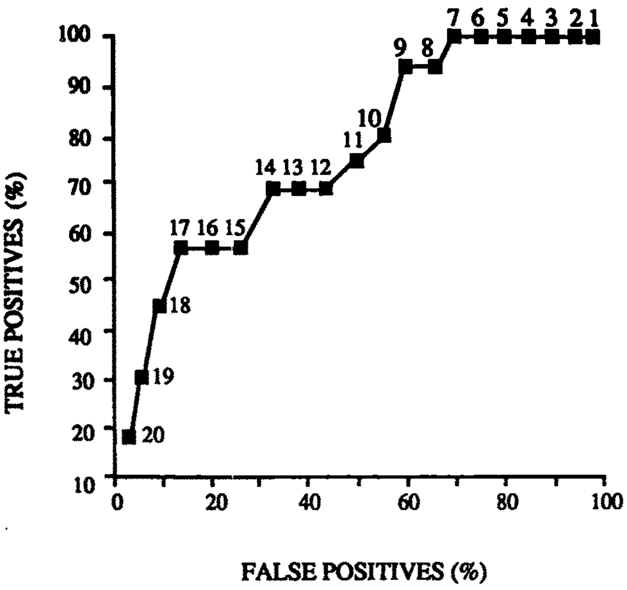
We examined the mean ages and Beck hopelessness and depression scores of those who committed suicide, those who died of natural causes, and living patients. In the case of one of the patients who committed suicide, who began treatment at the center on two separate occasions, self-report scores were available for the initial admission, which occurred in 1976, predating the period under study; consequently, the scores from the initial admission were used. Predictably, the patients who eventually died of natural causes were older as a group (mean±SD age=48.08±18.82 years) than the patients who committed suicide (40.35±11.61 years) and the living patients (36.01±12.31 years) (F=6.71, df=1, 1,955, $p<0.001$). As hypothesized, patients who committed suicide had higher scores on both the Beck Hopelessness Scale and the Beck Depression Inventory (mean±SD=15.29±4.47 and 30.59±11.52, respectively) than the patients who died of natural causes (7.33±5.21 and 20.92±8.64) and the living patients (9.98±5.42 and 20.14±9.88) (hopelessness scale: F=9.60, df=2, 1,955, $p<0.001$; depression inventory: F=9.44, df=2, 1,955, $p<0.001$).

### *The Beck Hopelessness and Depression Scales*

*Determination of optimal cutoff scores.* Optimal cutting scores for the two Beck scales were derived by applying a technique drawn from signal detection theory, the receiver operating characteristic curve (14). To construct such a curve, the percentage of positive responses in the presence of a signal ("hits" or true positives) is plotted against the percentage of positive responses in the absence of a signal ("false alarms" or false positives) for successive stimulus intensities. In terms of the present study, completed suicide is the signal and test score is the stimulus level.

Receiver operating characteristic curves for the Beck Hopelessness Scale and the Beck Depression Inventory are shown in figures 1 and 2. For situations in which maximizing *sensitivity* (the probability of suicide in subjects who are classified as at high risk by their test scores) and minimizing *specificity* (the probability of no suicide in subjects who are classified as at low risk by their test scores) are equally important, the optimal cutting score occurs at the point of furthest displacement of the curve. Because false negatives represent a loss of life, sensitivity is paramount in suicide prediction. The cutting score that maximizes sensitivity (at the expense of specificity) occurs where the distance from the vertical axis is minimized, while the distance to the horizontal axis is maximized. A Beck hopelessness score of 9 and a Beck depression score of 23 satisfy this criterion.

**FIGURE 1. Receiver Operating Characteristic Curve for the Relationship Between Scores on the Beck Hopelessness Scale and Ultimate Suicide Among 1,958 Psychiatric Outpatients**[a]

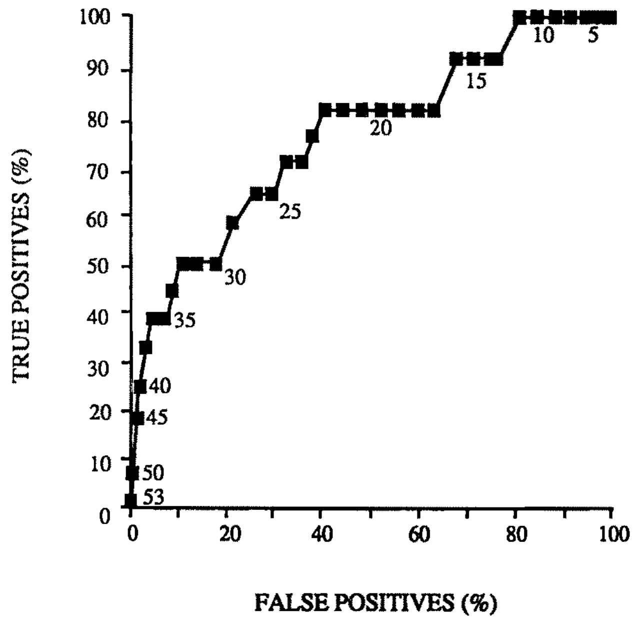


[a]The numbers within the graph represent scale scores used to identify patients at high risk for suicide. True positives are patients classified as being at high risk who did commit suicide. False positives are patients classified as being at high risk who did not commit suicide.

*Predictive validity.* The Beck hopelessness score of 9 or above defined a group (N=1,161) that included 16 (94.1%) of the 17 patients who committed suicide. The Beck depression cutoff score of 23 or above defined a smaller group (N=743) that included 13 (76.5%) of the patients who committed suicide. Although the Beck depression inventory had higher specificity (62.4%) than the Beck Hopelessness Scale (41.0%), the hopelessness scale had higher sensitivity (94.1%) than the depression inventory (76.5%). In addition, the high-risk group defined by the hopelessness scale (N=16 of 1,161) was 11.0 times more likely to commit suicide than the low-risk group (N=1 of 797); this was more than double the relative rate for the high- and low-risk groups defined by the depression inventory (N=13 of 743 and 4 of 1,215; odds ratio=5.3).

*Sensitivity to other risk factors.* We also wished to compare the 94.1% sensitivity rate found for the Beck Hopelessness Scale, by using a cutoff score of 9 or

**FIGURE 2. Receiver Operating Characteristic Curve for the Relationship Between Scores on the Beck Depression Inventory and Ultimate Suicide Among 1,958 Psychiatric Outpatients**[a]



[a]The numbers within the graph represent scale scores used to identify patients at high risk for suicide. True positives are patients classified as being at high risk who did commit suicide. False positives are patients classified as being at high risk who did not commit suicide.

above against the outpatient sensitivity rates for selected suicide risk factors that had been previously investigated in the inpatient study of the relationship between hopelessness to ultimate suicide (9). The risk factors included gender, previous suicide attempts, and a diagnosis of alcoholism. Of the 17 patients who eventually committed suicide (table 1), nine were men; the sensitivity rate for maleness was thus 52.9%. With respect to a history of previous suicide attempts, eight of the 17 patients who committed suicide had made at least one prior attempt; the sensitivity rate was 47.1%. Five of the 17 patients had received an alcohol-related diagnosis; the sensitivity rate for alcoholism was 29.4%. Obviously, the sensitivity rates for the three characteristics were substantially lower than that for the Beck Hopelessness Scale when a cutoff score of 9 or above was used (94.1%).

To gauge the specificity rates with respect to the previous characteristics, a subsample of 17 of the patients who did not commit suicide was chosen at random. In this subsample there were 10 men; the specificity rate for maleness was 41.2%. None of these patients had made a prior attempt or had a diagnosis of alcoholism; the specificity rates were both 100%. Therefore, the specificity rate for these past history variables was maximal, but the sensitivity rates were low compared to those of the Beck Hopelessness Scale and the Beck Depression Inventory.

**TABLE 1. Characteristics of 17 Outpatients Who Committed Suicide**

| Patient | Sex | Number of Prior Attempts | Alcohol-Related Diagnosis | Number of Therapy Sessions | Beck Hopelessness Scale Score |
|---|---|---|---|---|---|
| 1 | M | 2 | Yes | 0 | 10 |
| 2 | M | 0 | Yes | 15 | 14 |
| 3 | M | 0 | Yes | 3 | 17 |
| 4 | M | 0 | No | 7 | 11 |
| 5 | M | 3 | No | 4 | 20 |
| 6 | M | 0 | No | 14 | 14 |
| 7 | M | 0 | No | 0 | 18 |
| 8 | M | 0 | No | 25 | 18 |
| 9 | M | 2 | No | 0 | 9 |
| 10 | F | 1 | No | 0 | 20 |
| 11 | F | 2 | No | 0 | 19 |
| 12 | F | 6 | No | 13 | 20 |
| 13 | F | 0 | Yes | 8 | 19 |
| 14 | F | 0 | Yes | 14 | 9 |
| 15 | F | 1 | No | 0 | 18 |
| 16 | F | 1 | No | 0 | 17 |
| 17 | F | 0 | No | 1 | 7 |

## DISCUSSION

The present study was conducted specifically to ascertain whether level of hopelessness would be as predictive of eventual suicide in outpatients as it had been in the previously reported study of hospitalized patients with suicidal ideation (9). In the present study, patients who ultimately committed suicide scored significantly higher on both the Beck Hopelessness Scale and the Beck Depression Inventory than did patients who did not commit suicide and patients who died from natural causes. Moreover, an optimal cutting score on the hopelessness scale identified a group that was 11 times more likely to commit suicide than the low-risk group, and twice as likely to commit suicide as the high-risk and low-risk groups defined by the Beck Depression Inventory.

The present results replicate the earlier study of psychiatric inpatients by Beck et al. (9), which found a similar prediction rate with the same Beck Hopelessness Scale cutoff score of 9 or above. Together, these studies support the growing body of research which suggests that hopelessness is more directly related to suicide intent than depression alone (see Wetzel et al. [8] for a review). Fawcett et al. (15), for example, in a prospective study of a heterogeneous study of psychiatric patients, found that the hopelessness rating from the Schedule for Affective Disorders and Schizophrenia (16) was among the factors that differentiated the 25 patients who committed suicide from the 929 survivors. The relationship between hopelessness and suicide has also been demonstrated in schizophrenic patients, a group that is also at a significant risk for committing suicide (17). Drake and Cotton (18) found that ratings of hopelessness derived from the patients' charts, completed during hospitalization, accounted for the relationship between depression and suicide in a group of schizophrenic inpatients who eventually committed suicide: The hopelessness ratings were the best predictor of eventual suicide in their sample. The foregoing findings may explain the perplexity reported by clinicians who are confronted with unexpected suicidal deaths among discharged schizophrenic patients (19, 20), in the absence of assessment of hopelessness.

The present study and related research (9) represent a departure from previous investigations (21) of suicide prediction that have largely been limited to the study of demographic (e.g., socioeconomic status, unemployment status), organismic (e.g., gender, age), and past history (previous suicide attempts, alcoholism) variables. In contrast, hopelessness, as a measurable psychological dimension, represents an ongoing fluctuating index of relative suicide potential *within* these risk groups and provides a means for gauging the effects of clinical interventions. Further, in contrast to demographic variables, hopelessness is subject to direct clinical intervention.

One possible objection to the use of the Beck Hopelessness Scale in prediction is that in the present study it yielded a large proportion of false positives (59.0%). The nearly inevitable overinclusiveness of valid predictors of rare phenomena such as suicide was first demonstrated by Meehl and Rosen (22) and has since been widely discussed (23–25). However, it should be noted that the connotations of the terms "false negative" and "false positive" may not be completely appropriate in the present context. Generally, these terms are applied when a specific test is able or unable to demonstrate the *presence or absence* of a known disease, such as diabetes or tuberculosis. However, the Beck Hopelessness Scale attempts to identify the *potential* for fatal suicide attempts and not the behavior itself. Many persons with high scores on this scale may continue to be at risk for suicide beyond the observation period, even though they have not yet made a fatal suicide attempt.

In the interpretation of the results of the present study, hopelessness may best be construed as a *risk factor*—perhaps analogous to a history of smoking or elevated blood pressure as a predispositional factor in heart disease. In this connection, Murphy (17) has commented, "In the clinical context . . . the problem of false positives is not what it is in the laboratory. The decisions made are investigation and treatment decisions, involving much more than the issue of suicide. There is the continuing opportunity for feedback, and thus for modification of risk assessment and intervention."

In clinical practice, it would seem to be desirable to define and monitor patients at high risk for suicide. In addressing the issue of the economic cost of following a large number of high-risk patients who may or may not eventually commit suicide, Pallis et al. (26) stated:

> Since nearly two thirds of attempters are likely to receive inpatient or outpatient psychiatric care—a number far exceeding that classified high risk on any scale—the question is not whether to treat a high risk group but *how to ensure that it includes most of the true prospective suicides* [italics added] . . . by using [valid predictors of suicide], one is more likely to ensure that those at the highest risk would receive a closer follow-up or more appropriate attention. (p. 147)

Why does hopelessness serve as such a powerful predictor of eventual suicide? We believe that the intensity of hopelessness displayed during one depressive episode is indicative of the level that emerges in future episodes. In preliminary explorations of this issue, Beck (unpublished data, 1988) studied 59 outpatients at the center for cognitive therapy who sought treatment on two different occasions. Their mean±SD Beck hopelessness score at the index admission was 8.97±4.68, and their mean score at the time of the next admission to our clinic was 10.73±4.89. The correlation between index and reevaluation hopelessness scores was 0.51. Since the patients applied for readmission to the clinic because of recurrence of their index disorder or the appearance of a different disorder, the Beck hopelessness score at readmission was uniformly higher than at the time of the previous discharge from the clinic and may be regarded as indicative of a psychiatric disturbance or personal crisis rather than as a stable trait measure.

In this context, hopelessness as it occurs in depressed patients may be viewed as having state *and* trait characteristics. It rises and falls as the disorder develops and subsides. At the time of recurrence of the disorder it increases approximately to the same level as that reached at the time of the previous episode. Thus, a patient with severe depression but mild hopelessness or a patient with modest depression with marked hopelessness in one episode is prone to the same pattern in subsequent episodes. People who respond with marked hopelessness in one personal crisis will be likely to respond in the same way at the next crisis. Some individuals, however, are chronically hopeless regardless of whether they are depressed and are prone to suicidal wishes and behavior on a continuous basis. In such cases, hopelessness may constitute a stable belief, incorporating negative expectancies that are very resistant to change in suicide-prone patients.

In any event, hopelessness is an important clue that should alert clinicians to immediate or long-term suicide potential. It should be emphasized, however, that a comprehensive assessment of suicide risk should include, in addition to Beck hopelessness scores, such clinical predictors of suicide as the presence of an affective disorder, a high level of suicide ideation, a history of suicide attempts, a family history of suicide, a history of alcohol and drug abuse, and relevant demographic factors such as age, sex, and race. Future studies should be conducted to determine the applicability of the Beck Hopelessness Scale to a variety of other clinical populations, as well as to replicate the findings of the present investigation.

Finally, as mentioned earlier, hopelessness, unlike certain other predictors of suicide, such as age, sex, or race, is a characteristic that can be modified. A study by Rush et al. (27), in fact, showed that depressed patients treated with cognitive therapy showed a more rapid reduction in hopelessness scores than a comparison group of depressed patients treated with an antidepressant drug. Effective nonpharmacological treatments have an additional advantage in that they do not carry with them the additional risk of intentional overdose with antidepressant medication, as was the case with four of the 17 patients who committed suicide in the present study.

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# Tourette's Disorder in a Set of Reared-Apart Triplets: Genetic and Environmental Influences

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*Tourette's disorder was diagnosed in triplets reared apart from early infancy and reunited as adults. These data, combined with data on other family members, support the findings of research studies that have demonstrated genetic influences on Tourette's disorder.*

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Interest in genetic and environmental factors associated with Tourette's disorder has increased dramatically in recent years (1–4). It has been suggested that the mode of transmission is a major gene (5). Comings and Comings (6) have implicated chromosome 18 in a minor variant form of Tourette's disorder but have stated that the major gene has yet to be localized. Most researchers believe that genetic influences are important in the onset and progression of this disorder (5), although unspecified environmental influences may modify, or even check, its expression in some individuals. The less than perfect concordance for Tourette's disorder among monozygotic twins (3), who have all their genes in common, is powerful testimony to the involvement of nongenetic events in the development of the disorder.

The comparison of resemblance within sets of monozygotic twins to resemblance within sets of dizygotic twins is the classic twin design for evaluating genetic and environmental influences on normal and abnormal human growth and development. The only systematically conducted twin study of Tourette's disorder (3), in which strict diagnostic criteria were used, reported concordance of 53% for pairs of monozygotic twins and 8% for pairs of dizygotic twins. When the diagnostic criteria were broadened to include "any tics" in a set of twins, concordance rose to 77% for monozygotic pairs and 23% for dizygotic pairs. The researchers concluded that these findings supported the role of genetic factors in the development of Tourette's disorder. Twins in that analysis, however, were raised together in the same home, so the possibility of mutual imitation of tics and other behaviors related to Tourette's disorder cannot be definitively ruled out. Examining resemblance in characteristics of Tourette's disorder between adoptive relatives or between biological relatives reared apart would be an informative addition to the literature on Tourette's disorder.

The present report concerns the onset and progression of Tourette's disorder in a set of Swedish triplets reared apart from early infancy and reunited as adults. Medical and life history information on their adoptive and biological relatives is provided whenever possible.

The Minnesota Study of Twins Reared Apart is a comprehensive psychological and medical investigation of monozygotic and dizygotic twins reared apart from very early in life and then reunited as adults. Ninety-three sets of reared-apart twins and three sets of reared-apart triplets (and their spouses, when available) have participated in this project since its inception in March 1979 (7). The zygosity of all of the subjects has been determined on the basis of analyses of eight blood group systems, four serum proteins, six RBC enzymes, fingerprint ridge count, ponderal index, and cephalic index. The probability of misdiagnosis is less than 0.001 (8).

The triplets, who entered the study in 1981, consist of a pair of monozygotic females and a dizygotic male cotriplet. The triplets were separated from one another when they were approximately 2 months of age and were reared separately by adoptive families. Their first contact occurred when they were 47 years old. The period of time between their initial reunion and their assessment at the University of Minnesota was 25 months for the monozygotic female pair and 23

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months for the opposite-sex pairs. On the basis of an extensive life history interview, we estimated that the female monozygotic pair had approximately 108 contact days prior to assessment and the opposite-sex pairs had 7 contact days prior to assessment. One of the female triplets returned to Minneapolis for a brief visit 4 years after the initial assessment, during which time she completed additional life history, medical, and personality interviews and questionnaires and spent 1 night under observation in a sleep laboratory.

## METHOD

The triplets underwent extensive medical examinations and interviews as part of the standard medical assessment schedule for participants in the Minnesota Study of Twins Reared Apart. In addition, the triplets completed a Tourette's disorder survey, largely based on questionnaires composed by David L. Pauls, Ph.D., and Kenneth K. Kidd, Ph.D., of Yale University. These interview schedules were translated into Swedish by faculty members at the Department of Environmental Hygiene of the Karolinska Institute in Stockholm. The protocols were administered to the triplets by members of the nursing staff at the Karolinska Institute. The female triplets were interviewed in 1987, and the male cotriplet was interviewed in 1988.

We constructed a family pedigree that identified the triplets' biological relatives who had Tourette's disorder. Information on family members was provided by the triplets during the interviews in Sweden and by one of the female triplets during her second visit to Minneapolis. Several subsequent telephone interviews with this triplet were used to gather additional information. Some relatives were deceased, thus precluding direct examination. Descriptions of many of these relatives were provided, however, by more than one of the triplets, a procedure which improves diagnostic accuracy (9).

## RESULTS

As shown in the family pedigree (figure 1), the biological father and uncle were affected with Tourette's disorder, as are a male and a female child of one of the female triplets (the male child is now deceased because of a motor vehicle accident). It is emphasized that this pedigree chart includes biological relatives who were raised separately *and* together.

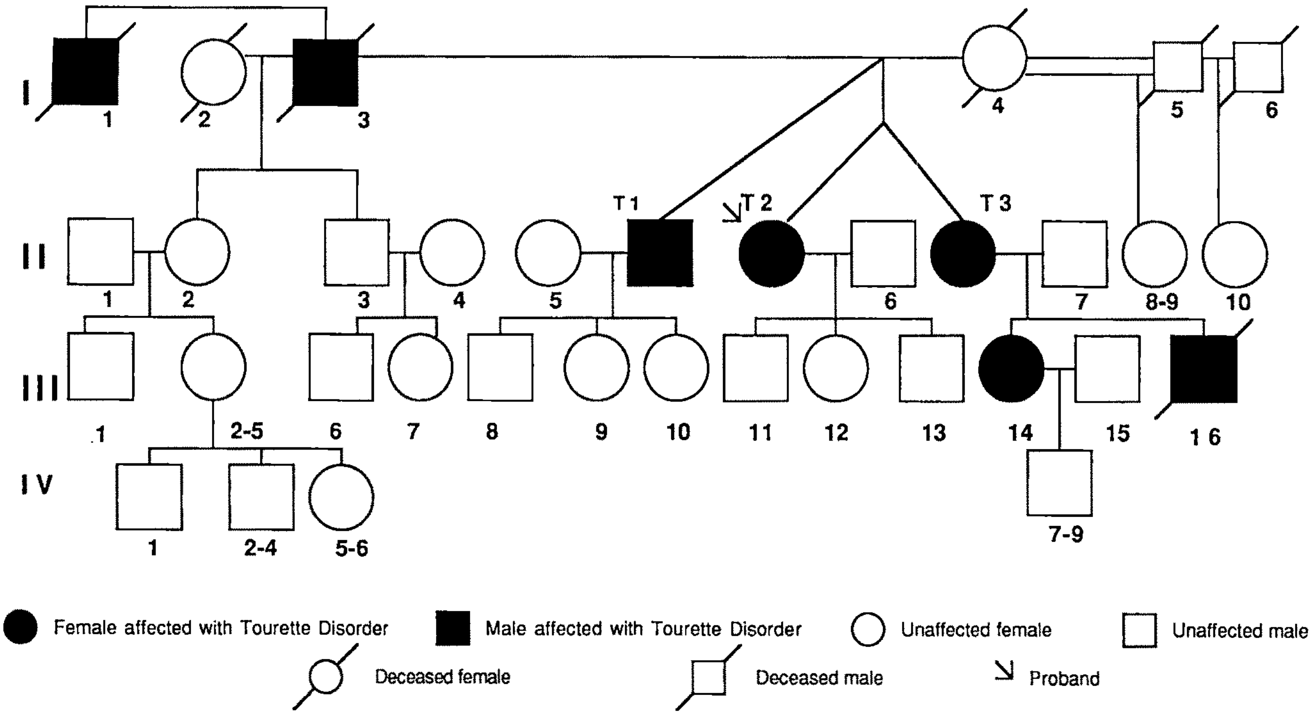
### Clinical Summaries

*Triplet 1 (firstborn).* This triplet is a 57-year-old divorced, right-handed man who is the dizygotic cotriplet of the monozygotic female pair. He provided a history of infrequent eye blinking, facial tics, and repetitive arm and finger movements that began when he was 4 years of age. When he was 12 years old, the facial tics and extremity movements disappeared, but the eye blinking has persisted until the present time. There is no history of phonic tics, rituals, compulsions, obsessional thinking, stuttering, hyperactivity, attention deficit disorder, or minimal brain dysfunction. He stated that he had to repeat the first year of school because of recurrent hospitalizations for involuntary movements and recalled that he experienced difficulty in learning to count. To his knowledge, a diagnosis of Tourette's disorder had not been made. There was no childhood history of use of antipsychotics or CNS stimulants or head trauma. On physical examination, his blood pressure was 166/110 mm Hg (supine) and 164/116 mm Hg (standing). Occasional repetitive blinking was observed. An ECG identified a left anterior fascicular block. Results of an echocardiographic examination and an exercise stress test were within normal limits.

*Triplet 2 (second-born).* This triplet is a 57-year-old divorced, right-handed woman who has experienced frequent motor and phonic tics since the age of 3 years. At present she is troubled by head jerks, shoulder jerks, and kicking leg movements that usually occur once every 1–4 minutes. In addition, she has much less frequent facial tics, arm movement tics, and head movements that appear once or twice an hour. Frequent eye blinking, which began when she was 3 years old, is no longer present. She also periodically grunts and has to clear her throat. Both motor and phonic tics characteristically appear and disappear over time and change in severity and frequency. A diagnosis of Tourette's disorder was made when the patient was 53 years old, during her second visit to the University of Minnesota. She provided a history of repetitive behavior, such as continuously turning her body to the right while walking down stairs, but these behaviors no longer persist. She also described the need to count to herself when she was younger, but this too no longer persists. There is no history of stuttering, hyperactivity, attention deficit disorder, minimal brain dysfunction, or learning disability. There is also no history of childhood use of antipsychotic agents or CNS stimulants, head trauma, or known CNS disease. A review of systems indicated that this triplet had a history of migraine headaches since the age of 30 years, orthostatic syncope since childhood, and labile hypertension. On physical examination, her blood pressure was 154/104 mm Hg (supine) and 150/102 mm Hg (standing). Involuntary movements of the face and feet were observed. Results of a brainstem auditory evoked response test, an echocardiographic examination, and an exercise stress test were within normal limits. Findings from an all-night sleep study were within normal limits, except for rare repetitive chin twitches that were seen during non-REM sleep and that were thought to possibly represent tics.

*Triplet 3 (third-born).* This triplet is a 57-year-old, right-handed woman who is the monozygotic twin of triplet 2. She also presents a history of motor and phonic tics that began sometime during childhood, before she was 5 years old. She currently experiences infrequent eye blinking and facial tics. When she is outdoors, she is aware of right-leg kicking that occurs once every 5–15 minutes. Shoulder jerks and arm movements that were present in childhood no longer occur. She describes both grunting and coughing during childhood, but these phonic tics are no longer present. The motor tics characteristically appear and disappear over time and change in severity. There is no history of rituals, compulsions, obsessional thinking, stuttering, hyperactivity, attention deficit disorder, minimal brain dysfunction, or any specific learning disability. There is also no childhood history of use of an-

**FIGURE 1. Family Pedigree of a Set of Triplets With Tourette's Disorder**[a]



[a] I. 1: Triplets' uncle, age ?, age at onset ? 2: Triplets' father's spouse, age ?, unspecified mental illness. 3: Triplets' father, estimated age 40 years at triplets' birth, age at onset ? 4: Triplets' mother, age 39 years at triplets' birth. 5: Triplets' mother's spouse, age ? 6: Adult male, alcoholic, age ?

II. 1: Spouse of 2, age ? 2: Triplets' paternal half-sister, age 59 years, migraine headaches. 3: Paternal half-brother, age 55 years. 4: Spouse of 3, age ? 5: Spouse of triplet 1, age 56 years. T1: Triplet 1, age 57 years, age at onset 4 years. T2: Triplet 2, age 57 years, age at onset 3 years. 6: Spouse of triplet 2, age 58 years. T3: Triplet 3, age 57 years, age at onset less than 5 years. 7: Spouse of triplet 3, age 58 years. 8–10: Triplets' three maternal half-sisters, ages 60, 59, and 56 years.

III. 1: Grandson of triplets' father, age 35 years. 2–5: Granddaughters of triplets' father, ages 33, 24, 21, and 20 years. 6 and 7: Grandchildren of triplets' father, estimated ages 20 and 14 years. 8–10: Son of triplet 1, age 32 years; daughter, age 31 years; daughter, age 29 years. 11–13: Son of triplet 2, age 32 years; daughter, age 29 years; son, age 25 years. 14: Daughter of triplet 3, age 33 years, onset in childhood, also affected with myasthenia gravis at 16–18 years, thyroid surgery at 25 years. 15: Spouse of 14, age ? 16: Son of triplet 3, age at death from a motor vehicle accident 24 years, age at onset 7–10 years.

IV. 1: Son of III3 (spouse not shown), age 2 years. 2–4: Sons of III4 (spouse not shown), ages 10, 9, and 5 years. 5 and 6: Daughters of III4, ages 12 and 7 years. 7–9: Sons of III14 (grandsons of triplet 3), ages 7, 5, and 3 years.

tipsychotics or CNS stimulants or head trauma. On evaluation in Minnesota, the patient provided a history of labile hypertension, migraine headaches since the age of 25 years, and orthostatic hypotension. On physical examination, her blood pressure was 168/114 mm Hg (supine) and 166/116 mm Hg (standing). No tics were observed. The results of an echocardiographic examination, a brainstem auditory evoked response test, and an exercise stress test were within normal limits.

## DISCUSSION

Each member of this triplet set meets *DSM-III* criteria for Tourette's disorder. The onset of Tourette's disorder occurred before they were 5 years of age, but also at least 1 year after each member had been placed in a separate foster family. Although vocalizations were a part of the symptom picture in the monozygotic female pair and continue to be manifest in one member, vocalizations did not develop in the male cotriplet. Triplet 2 gave a childhood history of repetitive behaviors that suggest the possibility of coexisting compulsive symptoms. It is not surprising that these features were absent in the other cotriplets because of the known variability of obsessive-compulsive disorder symptoms in Tourette's disorder (3, 9). Of interest is the history of migraine headaches in the monozygotic female pair and the presence of hypertension in all three triplets. Although the study by Price et al. (3) contained two sets of triplets, our report is, to our knowledge, the first detailed description of the presence and characteristics of Tourette's disorder in a set of triplets.

The presence of Tourette's disorder in an adult monozygotic/dizygotic set of triplets raised apart from early infancy provides unique evidence that genetic factors are important in the development of this disorder. The presence of this disorder among the first-degree relatives of the triplets, both those living together and those living apart, also underlines the importance of genetic effects. Outcomes from this case study are, therefore, consistent with the majority of twin and family studies that have implicated genetic factors in the etiology of this disorder. The somewhat variable symptom picture presented by the triplets may be associated with environmental events in the case of the monozygotic pair and both genetic and environmental events in the case of the dizygotic cotriplet. There are, however, no known environmental factors that can explain the symptom variability in this set of triplets. Other psychological and psychiatric studies of higher order monozygotic multiple births, such as that of the Genain quadruplets (10), also reveal an impressive degree of resemblance among partners with respect to social characteristics and mental illness, as well as behavioral variation associated with environmental sources.

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# The Prevalence of Anxiety Disorders in Patients With Chronic Obstructive Pulmonary Disease

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*Fifty consecutive outpatients with stable chronic obstructive pulmonary disease were evaluated for lifetime prevalence of psychiatric morbidity. Eight percent had a diagnosis of panic disorder. This finding suggests that this patient population should be monitored for panic disorder.*

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The psychosocial needs of patients with chronic obstructive pulmonary disease have been described (1). There have been reports of a high prevalence of major psychiatric disorders in this population (2–5). Yellowees et al. (6) detected a high rate of psychiatric morbidity (58%) in 50 consecutive patients with chronic obstructive pulmonary disease who were admitted to a respiratory unit; panic and other anxiety disorders (34%) were particularly prevalent. Various physiological hypotheses have been postulated as the etiological basis for such a high prevalence (7, 8).

This study describes the psychiatric morbidity in a consecutive outpatient sample with chronic obstructive pulmonary disease.

## METHOD

We evaluated 50 consecutive subjects with chronic obstructive pulmonary disease who were attending the Pulmonary Clinic of the Elmhurst Hospital Center, a municipal hospital in Queens, N.Y. These subjects had a significant chronic, irreversible airflow obstructive disorder due to chronic bronchitis, emphysema, or chronic asthma. They were not in acute respiratory distress and were receiving no medication that might account for psychiatric symptoms. None had an organic brain syndrome.

The 50 subjects (31 men and 19 women) in our study were interviewed over a period of 16 weeks—from November 1987 to March 1988. Their ages ranged from 44 to 85 years (mean±SD=64.96±9.70 years). The mean ages for the men and the women were 66.87±10.92 and 61.84±8.09 years, respectively. Twenty-one subjects were married, 12 were widowed, nine had never married, two were separated, and six were divorced.

Psychiatric interviews were conducted by using the Structured Clinical Interview for DSM-III-R (9). Forty-four of the 50 subjects (88%) were interviewed by one of the coauthors (R.K.), a preresident physician awaiting admission to a postgraduate residency program in psychiatry. R.K. was trained by the coauthor (B.K.) who interviewed the other six subjects. Information was also collected by interviewing the treating physicians and the relatives accompanying the subjects to the clinic.

## RESULTS

None of the subjects had a history of psychiatric treatment. Thirty-two subjects (64%) (22 men and 10 women) did not have any psychiatric diagnoses. Twenty-one (42%; 11 men and 10 women) had a past (N=7) or current (N=14) psychiatric disorder. Nine subjects (18%) had mood disorders; five had past and three had current episodes of major depression and one subject had a current episode of dysthymia. The male to female ratio for mood disorders was 1:2. Alcohol abuse was seen in four male subjects (8%) but in none of the female subjects. Two of these subjects were in remission. The overall prevalence of anxiety disorders was 16% (N=8); and the combined prevalence rate for panic disorder, with or without agoraphobia, amounted to 8% (N=4). All eight subjects were currently symptomatic; of the four subjects with panic disorder, only one had developed agoraphobia. The symptoms of panic attacks in these subjects with chronic obstructive pulmonary disease were not different from those in subjects with panic disorder without chronic obstructive pulmonary disease.

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## DISCUSSION

Although subjects with chronic obstructive pulmonary disease are chronically ill and are faced with major physical and social problems, lower rates of depression, dysthymic disorder, and alcohol dependence have been demonstrated in this population (10). In the present study 18% of the subjects with chronic obstructive pulmonary disease had a present or past diagnosis of a mood disorder; this figure is consistent with epidemiological surveys of the general population (11). Our finding that twice as many women as men had mood disorders was also expected. However, the lifetime prevalence rate for anxiety disorders (16%) and, in particular, for panic disorder (8%) is of interest. The prevalence rate for anxiety disorders in our study is comparable to what is found in the general population, i.e., 15% (11), whereas the prevalence rate for panic disorder is 5.3 times higher than what is found in the general population, i.e., 1.5% (11). The prevalence rates in the study by Yellowees et al. (6) were 34% and 24%, respectively, for anxiety disorders and panic disorder, rates that are higher than those found in the present study.

In 1984 Gorman et al. (12) suggested that $CO_2$ may cause panic by stimulating the locus ceruleus. In 1988 Gorman et al. (7) advanced the hypothesis that some subjects with panic disorder have $CO_2$ receptors, possibly in the brain stem, that are abnormally sensitive or at a low set point at least part of the time. When these receptors are triggered, a two-part process occurs. First, there is an extreme ventilatory response, which may be accompanied by a subjective sense of asphyxiation. Second, the ventilatory response induces hypocapnia and alkalosis, which produce light-headedness, dizziness, and disorientation and may accentuate the feeling of asphyxiation. It is possible that subjects with chronic obstructive pulmonary disease are more vulnerable to this response because they often are hypercapnic and the elevated $P_{CO2}$ may stimulate the locus ceruleus, triggering the two-part process clinically presenting as panic attacks.

It is not clear from our data whether those subjects with panic disorder had pulmonary symptoms before or after panic attacks began. We were careful to not confuse a panic attack with an episode of anxiety secondary to pulmonary dysfunction by not considering as a panic attack any anxiety that occurred in a situation commonly associated with a pulmonary problem, such as exertion. This distinction is important. The usual treatment for panic disorder (tricyclic antidepressants, alprazolam, or monoamine oxidase inhibitors) should not be neglected in subjects with chronic obstructive pulmonary disease.

Subjects with chronic obstructive pulmonary disease should be assessed carefully for panic disorder. If further research confirms the association of chronic obstructive pulmonary disease with panic disorder, this would support the hypothesis that a disturbance of $CO_2$ response is present in panic disorder.

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# Acute Postdisaster Psychiatric Disorders: Identification of Persons at Risk

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*This study examined the prevalence of four psychiatric disorders—posttraumatic stress disorder, major depression, generalized anxiety disorder, and alcohol abuse/dependence—in survivors of a jet plane crash into a hotel. Forty-six subjects were interviewed with the Diagnostic Interview Schedule/Disaster Supplement within 4–6 weeks of the event. More than half of the subjects met criteria for a psychiatric disorder after the disaster. More than two-thirds of the cases of acute postdisaster psychiatric disorders were predicted by identifying the subjects who had predisaster psychiatric histories. Predisaster psychiatric disorder predicted postdisaster psychopathology with a sensitivity of 72% and a specificity of 90%.*

(Am J Psychiatry 1990; 147:202–206)

There have been few systematic studies of the short-term effects of disasters. We have previously studied victims of several types of disasters approximately 1 year after the occurrence of the events and found prevalence rates of 14%–18% for psychiatric disorders in these subjects during the year since the disaster (1). The purpose of the current study was to examine acute postdisaster psychopathology. We hypothesized that examination of subjects in the acute phase would yield higher rates of psychopathology, since rates at the 1-year evaluations in our previous study were based on retrospective reporting. The major predictor of postdisaster psychopathology in our previous study was a history of a predisaster psychiatric condition; this finding has been supported by the work of others (2–4).

We chose to study a disaster which contained specific elements that have been found by other studies to contribute to the disaster impact. These elements include terror (i.e., threat of injury or death) and horror (i.e., exposure to grotesque stimuli) (5, 6); suddenness, unexpectedness, and unpreparedness (7, 8); scope and intensity (e.g., loss of lives and property destruction) (5, 7); and directness or degree of involvement with the disastrous event of the persons affected (2, 9). The following description of the event illustrates these elements.

## THE EVENT

At approximately 9:20 a.m. on Oct. 20, 1987, an Air Force jet fighter crashed into the lobby of a Ramada Inn in Indianapolis. The event was completely unexpected and without any warning. Although the hotel had been fully occupied the previous night, most of the guests had already checked out; the majority of the persons present were hotel employees. There were nine immediate fatalities, all employees. The remaining 22 employees were safely evacuated immediately after the crash, except for one who was hospitalized with burn injuries. There was one nonemployee fatality, a salesman who had stopped to use a hotel phone and who died of burn injuries approximately 1 week later.

Subjects reported considerable horror and terror associated with their experience. Survivors told stories of looking out a picture window to see the plane flying toward them, shrapnel from the plane blasting through walls five floors away, trapped victims crying and screaming for help and beating on walls as they died, bodies charred beyond recognition or blown to pieces, and a man running out of the hotel engulfed in flames.

Upon emerging to safety outside the burning hotel, many of the employees had the immediate impulse to go back to rescue those still trapped inside. Several tried but were immediately turned back by intense heat and smoke, only to stand helplessly, listening with horror to their co-workers' screams from inside as they perished. The scene outside was chaos, with the first arrivals of the 100 emergency and fire vehicles that ultimately responded, swarms of newspaper and television reporters, and crowds of onlookers and worried relatives. These crowds hampered frustrated friends

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and relatives in their frenzy to locate their loved ones. It was not until the following day that all the missing and dead were accounted for.

In addition to the immediate assistance provided by the Red Cross and neighboring businesses, there was a prompt response by the National Organization for Victims' Assistance, and group counseling was provided to all employees within a few days of the crash. As a result of the accident, the hotel was closed for what has proved to be an indefinite period. Thus, most of the surviving employees suffered loss of employment.

## METHOD

### *Subjects*

We elected to interview as many of the 62 surviving hotel employees as possible. We decided not to include the hotel guests in the study, since most had already scattered and would be difficult to locate because their hotel registrations had been burned in the fire. The community of hotel employees was close-knit, which made it likely that even those not present at the time of the crash would have experienced psychological sequelae. The inclusion of these off-site employees allowed a unique opportunity to examine the relation between level of exposure to the disaster and degree of emotional upset.

Aided by the cooperation of the hotel managers, we were able to contact 53 of the employees and invite them to participate in the study. Nine individuals (15%) could not be located because of complications resulting from the disaster (destroyed records, newly unemployed victims relocating for financial reasons). Most of these were contract workers who had had limited contact with the rest of the employees. Only one of the unlocated subjects had been in the hotel at the time of the crash.

Seven (13%) of the 53 employees we contacted refused to participate; four of these had been in the hotel at the time of the disaster. Several indicated that they believed it would be too upsetting to talk about the experience, and one had been advised by a lawyer not to talk to anyone. A few refusals seemed primarily due to employees' lack of involvement with the disaster or its low impact on them. A total of 46 (74%) of the 62 surviving employees were interviewed; these were fairly evenly distributed among those who had been at the hotel (17 of 22, or 77%) and those who had not (29 of 40, or 73%).

### *Instrument*

Subjects were interviewed about their psychiatric and social status with a modified version of the Diagnostic Interview Schedule/Disaster Supplement (10). This interview was designed for the Epidemiologic Catchment Area Hazards Study funded by NIMH (1) and has been used by investigators in several recent disaster studies. It elicits information about the disaster experience and individuals' perceptions of the event, use of formal and informal support systems, behavioral response to the traumatic event, and 15 *DSM-III* diagnoses selected for their relevance to the disaster experience. In this paper we focus on four diagnoses: posttraumatic stress disorder (PTSD), major depression, generalized anxiety disorder, and alcohol abuse/dependence.

For each disorder that was ascertained to have occurred, the subject's age at onset and age at last symptom were obtained, thus providing information on lifetime as well as current psychiatric status. Onset and recency of each positive symptom of the relevant diagnoses were also obtained, giving us information regarding the presence or absence of each symptom during the interval between the disaster and the interview as well as before the disaster.

The majority of the interviews were conducted face to face and were completed 4–6 weeks after the disastrous event. For various reasons, in a few instances face-to-face interviews could not be scheduled, and the interviews were completed by telephone. The interviews were conducted by the authors and a research assistant and lasted approximately 90 minutes. Each subject was offered $10.00 for participating.

### *Data Analysis*

An effort was made to examine the relation between degree of exposure to the plane crash and development of psychopathology in the acute postdisaster phase. To analyze the data from this perspective, subjects were grouped into three categories: "hit" or on site (N=17), "near hit" (N=12), and "miss" (N=17). The near-hit group included those who had originally been scheduled to be at work at the time of the crash but for some reason—oversleeping, illness, canceled meeting—were not there. The separation of subjects into two off-site subgroups was done because all of the subjects in the near-hit subgroup had independently volunteered the information that they felt they were in a very different position from the rest of the off-site group, and many claimed that they felt especially upset because they "should have been there." The miss subgroup consisted of those employees who had not been at the hotel because they had not been scheduled to be at work that day (e.g., the nighttime bartender and entertainment employees). However, on all measures examined in the study, tests of significance showed no difference between the near-hit and the miss subgroups; hence, in this paper the results are shown only for comparisons of the on-site group and the combined off-site subgroups.

We constructed 2×2 tables to organize the data. Chi-square tests were used to assess the level of significance when all expected frequencies were greater than 5. Otherwise, Fisher exact tests were performed.

**TABLE 1. Demographic Characteristics of Hotel Employees Who Survived a Plane Crash Into a Hotel**

| Item | On-Site Employees[a] (N=17) |  | Off-Site Employees[b] (N=29) |  | All Employees (N=46) |  |
|---|---|---|---|---|---|---|
|  | N | % | N | % | N | % |
| Sex |  |  |  |  |  |  |
| Male | 5 | 29 | 12 | 41 | 17 | 37 |
| Female | 12 | 71 | 17 | 59 | 29 | 63 |
| Race |  |  |  |  |  |  |
| White | 16 | 94 | 26 | 90 | 42 | 91 |
| Black | 1 | 6 | 3 | 10 | 4 | 9 |
| Marital status |  |  |  |  |  |  |
| Married | 13 | 76 | 7 | 24 | 20 | 43 |
| Divorced/separated | 0 | 0 | 6 | 21 | 6 | 13 |
| Single | 4 | 24 | 15 | 52 | 19 | 41 |
| Widowed | 0 | 0 | 1 | 3 | 1 | 2 |

[a] Employees who were in the hotel when the plane crashed.
[b] Employees who were not in the hotel when the plane crashed.

**TABLE 2. Rates of Psychiatric Diagnoses in Hotel Employees Who Survived a Plane Crash Into a Hotel**

| Diagnosis | On-Site Employees[a] (N=17) |  | Off-Site Employees[b] (N=29) |  | All Employees (N=46) |  |
|---|---|---|---|---|---|---|
|  | N | % | N | % | N | % |
| All diagnoses since disaster (prevalence) |  |  |  |  |  |  |
| PTSD | 5 | 29 | 5 | 17 | 10 | 22 |
| Alcohol abuse/dependence | 2 | 12 | 4 | 14 | 6 | 13 |
| Depression | 7 | 41 | 12 | 41 | 19 | 41 |
| Generalized anxiety disorder | 5 | 29 | 4 | 14 | 9 | 20 |
| New diagnoses since disaster (incidence) |  |  |  |  |  |  |
| PTSD | 5 | 29 | 2 | 7 | 7 | 15 |
| Alcohol abuse/dependence | 2 | 12 | 0 | 0 | 2 | 4 |
| Depression | 4 | 24 | 5 | 17 | 9 | 20 |
| Generalized anxiety disorder | 3 | 18 | 2 | 7 | 5 | 11 |
| Diagnoses present before and after disaster (persistence) |  |  |  |  |  |  |
| PTSD | 0 | 0 | 3 | 10 | 3 | 7 |
| Alcohol abuse/dependence | 0 | 0 | 4 | 14 | 4 | 9 |
| Depression | 3 | 18 | 7 | 24 | 10 | 22 |
| Generalized anxiety disorder | 2 | 12 | 2 | 7 | 4 | 9 |

[a] Employees who were in the hotel when the plane crashed.
[b] Employees who were not in the hotel when the plane crashed.

## RESULTS

Two-thirds of the subjects were female and most were Caucasian, with a mean±SD age of 29.2±10.8 years (for on-site subjects, 30.1±11.4; for off-site subjects, 28.8±10.6). Sex ratios, race, and age were similar in the on-site and off-site groups (see table 1). The sample contained a sizable number of part-time and unskilled workers, which may help to explain the relatively young age of the groups. More on-site subjects than off-site subjects were married. The mean±SD number of years of education was 11.8±2.1 (for on-site subjects, 11.6±1.1; for off-site subjects, 12.0±2.6).

Subjects were asked how upset they had been after the plane crash, and how much they felt they had been harmed. Perceived degree of upset was scored as high ("very upset") by most (83%, N=38) of the respondents. It is not surprising that 100% of the 17 on-site subjects reported that they were very upset. Seventy-two percent (N=21) of the 29 off-site subjects reported feeling very upset. The difference fell short of statistical significance (p=0.07). Over 70% of the subjects in the on-site group and over half of those in the off-site group believed that the disaster had caused them a great deal of harm; the difference between the two groups on this measure was not significant. Only 26% (N=12) of the subjects felt that they had completely recovered after 1 month, and the on-site victims (12%, N=2) were significantly less likely than the off-site subjects (34%, N=10) to report that they had made a full recovery ($p \leq 0.05$).

Fifty-four percent (N=25) of the subjects met the *DSM-III* criteria for psychiatric diagnoses following the disaster, and the rates were only slightly higher in the on-site group (59%, N=10) than in the off-site group (52%, N=15) (Fisher's exact test, p=0.64).

Thirty-three percent (N=15) of the sample developed a new diagnosis—PTSD, alcohol abuse/dependence, depression, and generalized anxiety disorder—following the disaster (i.e., an incident diagnosis in an individual not reporting symptoms of that specific disorder before the disaster). Fifty-three percent (N=9) of the on-site group met criteria for postdisaster incident diagnoses, while only 21% (N=6) of the off-site group did. A much higher proportion of the off-site subjects (48%) than of the on-site subjects (35%) had histories of predisaster psychiatric disorders and when these individuals were removed from the analysis, there was no statistically significant difference in incident diagnoses between the two groups.

Twenty-two percent (N=10) of all the subjects met criteria for PTSD after the disaster. Most cases of postdisaster PTSD were new cases in subjects without histories of PTSD. All cases of PTSD in on-site victims appeared for the first time following the disaster; this pattern was not seen in the off-site subjects, whose PTSD represented a recurrence of a previous PTSD episode as frequently as it represented new development of the disorder. None of the on-site victims recalled any history of a PTSD episode, but 14% (N=4) of the off-site group recalled a prior episode.

Twenty percent (N=9) of the subjects had been abusing or dependent on alcohol before the disaster; about half this number were actively abusing alcohol after the disaster (table 2). Those abusing alcohol after the disaster were not necessarily the same ones who had histories of alcohol abuse. The two subjects who developed alcohol abuse were both in the on-site group. About half the alcohol abuse cases also met criteria for dependence. The prevalence of postdisaster alcohol diagnoses was not significantly different in the on-site and off-site groups.

Depression was the most common postdisaster diagnosis, with more than 40% of the subjects meeting the criteria (table 2). There was no significant difference in rates of depression between on-site and off-site subjects. (Although it is not shown in table 2, male subjects were slightly overrepresented in depressive cases.) Approximately 22% (N=10) of the subjects met criteria for a previous episode of depression, and on-site victims recalled fewer past depressive episodes than off-site subjects. All 10 cases of preexisting depression recurred or persisted after the disaster.

The overall postdisaster prevalence rate of generalized anxiety disorder was 20%. Although on-site victims had more than twice the rate of the off-site victims (table 2), this difference was not statistically significant. Prevalence did not vary by sex. In on-site subjects anxiety disorders appeared for the first time after the disaster about as often as they represented a recurrence.

There was considerable overlap in the postdisaster prevalence of psychiatric disorders. PTSD occurred in conjunction with one of the other nonalcohol diagnoses four times more frequently than it did alone. Generalized anxiety disorder occurred in conjunction with another nonalcohol diagnosis eight times more frequently than it did alone. Depression was the most likely of the disorders to occur in the absence of another nonalcohol diagnosis, which was the case in 42% of the 19 subjects with depression. Those few subjects who were abusing alcohol almost always met the criteria for at least one of the other diagnoses.

Subjects' perceptions of degree of harm were not objectively supported by the presence of psychiatric diagnoses in those who perceived the greatest harm. Subjective reports of degree of recovery, however, did parallel the findings of psychopathology in these subjects. All subjects who reported that they had not at least partially recovered had psychiatric diagnoses. Surprisingly, almost one-fourth (N=6) of the 25 with at least one diagnosis felt fully recovered despite their diagnosable psychopathology. This unusual subset averaged two diagnoses per subject; the most common diagnosis in this group was depression, which occurred in five of the six subjects.

Ninety percent (N=18) of the 20 subjects with previous psychiatric diagnoses experienced diagnosable postdisaster psychopathology, while slightly over one-fourth (N=7) of the 26 without previous diagnoses experienced postdisaster psychopathology (table 3). Only two (10%) of the 20 subjects with predisaster diagnoses were free of psychiatric disorder following the disaster, and these two subjects were in the off-site group. Many individuals without prior diagnoses developed psychiatric disorders after the plane crash, but more frequently they remained free of psychiatric disorder, and this held for both groups. Overall, more than two-thirds of the postdisaster psychiatric disorders occurred in individuals who had prior psychiatric diagnoses.

**TABLE 3. Preexisting and Postdisaster Psychiatric Diagnoses of Hotel Employees Who Survived a Plane Crash Into a Hotel**

| | Preexisting Diagnoses | | |
|---|---|---|---|
| Postdisaster Diagnoses | None | One or More | Total |
| On-site employees[a] (N=17) | 11 | 6 | 17 |
| None | 7 | 0 | 7 |
| One or more | 4 | 6 | 10 |
| Off-site employees[b] (N=29) | 15 | 14 | 29 |
| None | 12 | 2 | 14 |
| One or more | 3 | 12 | 15 |
| All employees (N=46) | 26 | 20 | 46 |
| None | 19 | 2 | 21 |
| One or more | 7 | 18 | 25 |

[a]Employees who were in the hotel when the plane crashed.
[b]Employees who were not in the hotel when the plane crashed.

Of the 25 subjects with postdisaster diagnoses, 18 had predisaster diagnoses. Thus, predisaster diagnosis was a strong predictor, with a sensitivity of 72%. Of the 21 subjects without postdisaster diagnoses, 19 had no predisaster diagnosis, for a specificity of 90%. Given the limited size of this sample, however, the confidence intervals for these measurements are large.

## DISCUSSION

The findings of our preliminary data analysis show that after a disaster which has strong elements of terror and horror, survivors report experiencing high rates of upset and feelings of harm, but these subjective reports do not correlate statistically with objective evidence of psychopathology (i.e., with psychiatric diagnoses). On-site subjects, who were directly exposed to the disastrous event, felt significantly less recovered than their off-site co-workers 1 month after the event. Thus, degree of exposure was correlated with subjective reports of distress, but objective diagnostic prevalence data were not.

More than half of the study subjects met criteria for psychiatric diagnoses after the disaster, and 72% of these were individuals with predisaster histories of psychiatric disorder. Our calculations of sensitivity and specificity support the findings of our previous work as well as that of investigators of other disasters who have found that previous psychiatric disorder is a strong predictor of posttrauma psychopathology. The fact that the high-exposure (on-site) group in our study started out in better psychiatric health but ended up with more psychopathology than the low-exposure group suggests that the severity of the traumatic experience may have played a part. Indeed, Hocking (11) has hypothesized that in situations approaching the most extreme points of the stress spectrum, all subjects will eventually break down. Ursano (12), in a study of Vietnam prisoners of war, found that a history of psychiatric disturbance was not a necessary antecedent of posttrauma psychopathology. The findings of our study support Hocking's theory and Ursano's findings and suggest at most a mild "dose-response" effect in the two exposure groups.

If substantiated by replication in other studies, these findings will provide useful information to disaster workers. To focus their limited resources on those in greatest need, they must identify the target population at greatest risk. For example, since we found a 100% recurrence rate of preexisting depressive disorders in the high-exposure group and a high rate in the off-site group, persons who report preexisting depressive disorders represent a clearly identifiable target population at great risk for postdisaster depression. Psychiatric intervention would be especially important for this group and for individuals with a history of any psychiatric disorder.

Cases of PTSD tended to arise for the first time after the disaster in subjects without predisaster histories of the disorder, especially in the high-exposure group. Interestingly, the subjects were often able to tell us how they were doing: all subjects who reported that they had not at least partially recovered met the criteria for a postdisaster diagnosis.

Often overlooked in disaster research are findings related to good health. Many individuals with postdisaster psychiatric disorders had no psychiatric history prior to the event (almost one-third of the 25 in this sample), and many exposed individuals do not develop a postdisaster disorder (almost half in this study did not). This finding may help to reorient clinicians to issues of health rather than illness following disaster.

Our findings are not an end point; they represent a starting point for future research. Although the finding that acute postdisaster psychopathology occurs in a predictable pattern is useful, further follow-up studies tracing the course of symptoms and the process of recovery over time will be equally important to identify the needs of disaster victims in later phases of their recovery.

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# Emergence of Intense Suicidal Preoccupation During Fluoxetine Treatment

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*Six depressed patients free of recent serious suicidal ideation developed intense, violent suicidal preoccupation after 2–7 weeks of fluoxetine treatment. This state persisted for as little as 3 days to as long as 3 months after discontinuation of fluoxetine. None of these patients had ever experienced a similar state during treatment with any other psychotropic drug.*

(Am J Psychiatry 1990; 147:207–210)

Antidepressants occasionally promote suicidal actions in severely depressed patients by enhancing drive and counteracting psychomotor retardation (1). However, standard antidepressants are not known to induce severe and persistent suicidal ideation in depressed patients free of such thoughts before treatment. We have recently observed several complex patients who appear to have had serious paradoxical responses to fluoxetine that were characterized by intense, violent suicidal thoughts.

## CASE REPORTS

*Case 1.* Ms. A, a 62-year-old woman, had a 17-year history of major depression with melancholia. Previously she had been cheerful, outgoing, and successful in her profession. She had no evidence of personality disorder but occasionally abused alcohol. Previous treatment trials had included most available tricyclic antidepressants, phenelzine, tranylcypromine, trazodone, alprazolam, carbamazepine, lithium, methylphenidate, and five investigational compounds. Ms. A had had a moderate response to a course of ECT and to a trial of amoxapine, but the benefits were short lived. Her symptoms included fatigue, lethargy, hypersomnia, psychomotor retardation, anhedonia, guilt, and occasional passive suicidal thoughts without any suicide attempts.

Before treatment with fluoxetine, Ms. A had received a second trial of amoxapine, with lorazepam and temazepam available for sedation. After a 4-week medication-free period and with a baseline score on the Hamilton depression rating scale (2) of 23, she was enrolled in a therapeutic study of fluoxetine. She received 20 mg/day in the first week, 40 mg/day on days 8–10, and 60 mg/day thereafter. On day 11 she began to experience forced obsessional suicidal thoughts consisting of intense and incessant wishes to kill herself and described by Ms. A as "uniquely bad." This led to such significant anxiety, fear, and turbulence that she felt "death would be a welcome result." She also felt like "jumping out of her skin" but had no signs of motor restlessness. Her depressive symptoms and Hamilton depression score remained the same, except for these intolerable forced suicidal thoughts. Fluoxetine treatment was discontinued, and after 3 days the intensity and obsessional quality of her suicidal thoughts abated.

*Case 2.* Mr. B, a 39-year-old successful professional man, had a 21-year history of dysthymia and episodic major depression, but no previous suicidal ideation. He had managed successfully with psychotherapy until 2 years ago, when his depression worsened after a divorce and a medication trial was initiated. Isocarboxazid (50 mg/day) enhanced his energy, mood, and self-confidence and diminished his anger and irritability. Six months later tolerance emerged and Mr. B developed hyperphagia, anergia, poor concentration, diminished libido, and passive suicidal thoughts. After a 2-week washout, fluoxetine was initiated at a dose of 20 mg every other day for 7 days, then daily. One month later his Hamilton depression score was 32 and he had several new complaints, including anxious unproductive energy, nausea, severe loss of appetite, and abulia. Most alarming, however, was the emergence of nearly constant suicidal preoccupation, violent self-destructive fantasies, and Mr. B's resignation to the inevitability of suicide. This was such a dramatic change in his behavior and attitude that both his elderly mother and his former wife made emergency telephone calls to his treaters because they were worried about his risk for suicide. Two weeks of lithium potentiation (600 mg/day) enhanced his energy slightly, but he remained intensely suicidal, so both agents were discontinued. During the next 3 months, trials of imipramine, doxepin, and methylphenidate provided little relief, and Mr. B's intense suicidal thoughts persisted until 2 weeks after treatment with tranylcypromine was initiated. Despite ongoing depression and a Hamilton depression score of 16, all traces of active suicidal ideation vanished.

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*Case 3.* Ms. C, a 19-year-old college freshman, was hospitalized for the first time with symptoms of depression, paranoia, bulimia, agoraphobia, and dissociation. She had a history of mild suicidal gestures that had been managed without hospitalization. Past medications included haloperidol and trifluoperazine, which alleviated the paranoia (but led to substantial extrapyramidal side effects), and imipramine, which relieved her depression.

In the hospital Ms. C experienced occasional suicidal thoughts but had no active plan or intent. Perphenazine (4–12 mg/day) alleviated her paranoia and enabled her to sustain meaningful relationships and to obtain employment after 3 months. However, depression emerged and treatment with tranylcypromine (20–30 mg/day) was initiated, but it was discontinued because of orthostatic hypotension. Passive suicidal ideation reemerged, along with irritability, hopelessness, and increased purging.

Two weeks later, fluoxetine (20 mg/day) was added to the perphenazine (12–20 mg/day). During the next 2 weeks Ms. C became more paranoid, depressed, and irritable, and she developed disturbing self-destructive thoughts but no active suicidality. The fluoxetine dose was increased to 40 mg/day, and the perphenazine dose was lowered from 20 to 16 mg/day because of worsening akathisia. After 3 weeks Ms. C impulsively ran away and superficially scratched her forearms. Over the next week she became more depressed and preoccupied with thoughts of death. After 1 month of treatment, the dose of fluoxetine was increased to 60 mg/day. She then suffered from hypersomnia, poor concentration, diurnal variation, anhedonia, anergy, fatigue, and increased binging and purging. During week 5 she escaped from the hospital and planned to commit suicide, but she was located by hospital security staff. After the fluoxetine dose was increased to 80 mg/day she became violent, banging her head and mutilating herself, and physical restraint was necessary. Although lithium carbonate augmentation was briefly attempted, fluoxetine treatment was discontinued after a total of 6 weeks.

During the next week Ms. C lacerated her forearms and required emergency room treatment. Although less labile, she remained extremely suicidal and required restraint periodically. Her active self-destructive urges abated 1 month after fluoxetine treatment was stopped, although intermittent suicidal ideation persisted. Improvement continued over the next 2 months with perphenazine treatment (32 mg/day), although Ms. C scratched her arms after learning of the sale of her family home. Nortriptyline was added to her regimen, and over the next month she had no further suicidal ideas or intention. Her ability to function markedly improved, and she was discharged 3 months after fluoxetine treatment was discontinued.

*Case 4.* Ms. D, a 39-year-old former executive, had a history of recurrent major depression, episodic alcohol abuse (in remission), and borderline personality disorder. During the last 8 years she received aggressive pharmacological treatment with little benefit. Trials of monoamine oxidase inhibitors (MAOIs) were moderately successful but were accompanied by intolerable side effects, and ECT produced marked but short-lived improvement. Ms. D had been intermittently suicidal and had taken drug overdoses on three occasions while enraged. However, each suicide attempt, although serious, was a direct request for help, and her suicidal state dissipated rapidly after hospitalization.

Before treatment with fluoxetine, Ms. D had relapsed into major depression after a transient recovery that had followed discontinuation of nortriptyline treatment. Her symptoms included hypersomnia, social withdrawal, irritability, and psychomotor retardation, without suicidal ideation. Fluoxetine treatment was started at a dose of 20 mg/day. Two weeks later, Ms. D was more depressed and was experiencing extreme fatigue, daytime sedation, and persistent negative thoughts that progressed to intense suicidal ideation. For the first time she contemplated obtaining a gun to commit suicide. Her treatment was also complicated by the development of a truncal erythematous pruritic rash, which was initially treated with dexamethasone, then terfenadine. The fluoxetine dose was gradually increased to 60 mg/day over 2 months. She began to think fluoxetine was a "deadly drug," and she developed a strong desire to drink. Despite her poor response, she wished to continue taking fluoxetine, as she knew of other patients who had responded to it only after months of treatment.

By her third month of treatment, at a dose of 80 mg/day, Ms. D remained profoundly depressed. Anger, frustration, and persistent suicidal ideation predominated. After 5 years of sobriety, she drank. Fluoxetine treatment was discontinued, but her symptoms intensified and culminated 2 weeks later in a secret suicide attempt involving diazepam and alcohol. In contrast to her prior attempts, when she had immediately called for help, she was discovered by her sister only when her telephone went unanswered. In the hospital, she disclosed the full extent of her self-destructive thoughts. They included severe suicidal ruminations, dissociative feelings, and the belief that she could not fight or control her suicidal impulses. She believed that fluoxetine would enable her to successfully commit suicide, and she hid this information from others.

In the hospital, Ms. D's profound distress and agitation were partially relieved by chlorprothixene, a neuroleptic with prominent serotonin antagonist effects (3). Her suicidal thoughts diminished over 3 weeks, but profound fatigue and psychomotor retardation returned. Eight weeks after the discontinuation of fluoxetine treatment, tranylcypromine was added to the chlorprothixene, her residual suicidal ideation remitted, and she improved sufficiently to be discharged.

*Case 5.* Ms. E, a 39-year-old woman with major depression, borderline personality disorder, and temporal lobe epilepsy, had been successfully treated with MAOIs, carbamazepine (1200 mg/day), and clonazepam (0.5 mg every other day). Persistent suicidal thoughts predated pharmacological treatment but had been absent for at least 2 years. She had never made any suicide attempts. Unfortunately, MAOI therapy was complicated by weight gain and virtual anorgasmia. Fluoxetine was substituted for isocarboxazid after a washout period of 2 weeks; the initial dose was 20 mg/day, which was increased after 3 weeks to 40 mg/day. During this time Ms. E was depressed, apathetic, fatigued, and hypersomnolent. Suicidal thoughts reemerged after years of their absence. Pemoline (37.5 mg/day) was added to increase her energy, but the suicidal ideation worsened and she began to fantasize about purchasing a gun for the first time. The fluoxetine dose was increased to 60 mg/day in the sixth week and to 80 mg/day in the eighth week. Ms. E then complained of prominent dissociative symptoms, sedation, and abulia. Fluoxetine treatment was discontinued, and methylphenidate (5 mg/day) was substituted for the pemoline. Although Ms. E felt less depressed, her severe obsessive suicidal thoughts continued. In contrast to her past experience with suicidal feelings, she now embraced these impulses and hid them from the clinicians. She checked the *Physician's Desk Reference* to see if any of her medications were particularly lethal, and she repeatedly poured out her pills and struggled over taking them. Eleven days after discontinuation of fluoxetine, her suicidal thoughts diminished, but she remained quite depressed. Isocarboxazid treatment was resumed 6 weeks later, and after 1 month her energy, sociability, work performance, and mood were substantially improved and she had no more suicidal thoughts.

*Case 6.* Ms. F, a 30-year-old woman, had a history of bipolar disorder, multiple personality disorder, pseudotumor cerebri, hypothyroidism secondary to propylthiouracil treatment, and an abnormal EEG. Her history included three significant suicide gestures, the first at age 17 and the last 5 years ago. Intermittent suicidal thoughts had continued during the past 5 years. Past medication trials included tricyclic antidepressants, which were of little benefit, and MAOIs, which led to significant therapeutic responses.

With daily doses of haloperidol (4 mg), carbamazepine (600 mg), clonidine (0.4 mg), thyroxine (150 μg), acetazolamide (750 mg), and diazepam (40 mg), severe anxiety and depression emerged, with self-loathing, anergy, fatigue, hopelessness, suicidal ideation, and social withdrawal. Fluoxetine was added to her complex regimen, and the dose was gradually increased to 40 mg/day over 1 month. After Ms. F developed an erythematous rash, her fluoxetine dose was decreased to 20 mg/day. During this period her condition worsened, with increased feelings of anxiety, dissociation, lethargy, and incapacity. A brief attempt to potentiate treatment by adding pemoline (18.75 mg/day) was unsuccessful. By week 7 she was severely depressed, detached, withdrawn, restless, and agitated; fluoxetine was discontinued. Two days later her internal personalities started shouting at her to commit suicide. During the next 2 weeks she remained depressed and had a Hamilton depression score of 28; hospitalization was recommended, but she declined. Her self-destructiveness continued to intensify; she planned a lethal overdose and put a loaded gun to her head. With family intervention and daily telephone contact, she continued in outpatient treatment. She remained depressed, anxious, and intensely suicidal for 1 month after fluoxetine treatment was abandoned. The severity of her self-destructive thoughts and her need to act on them then abated.

## DISCUSSION

Five depressed outpatients and one inpatient, 19–62

suicidal ideation while receiving only fluoxetine. The remainder were taking a variety of other medications, which included carbamazepine (cases 5 and 6), neuroleptics (cases 3 and 6), benzodiazepines (cases 5 and 6), and thyroxine (case 6). Three patients also received stimulant trials to combat fluoxetine-induced anergia (cases 4–6), and lithium potentiation was unsuccessful in two patients after suicidal preoccupation had emerged (cases 2 and 3). All patients had previously been treated with MAOIs, and for three (cases 2, 3, and 5), an MAOI had been the last treatment before fluoxetine. Resumption of MAOI treatment (after at least a 6-week fluoxetine washout period) appeared to result in rapid abatement of persistent suicidal ideation in the three cases in which this was tried (cases 2, 4, and 5).

In no case was there evidence that strong preexisting self-destructive urges were activated and energized by fluoxetine. No patient was actively suicidal at the time fluoxetine treatment began. Rather, all were hopeful and optimistic, and the strong obsessive suicidal thoughts apparently emerged de novo after weeks or months of treatment. In four patients (cases 2 and 4–6), these thoughts were accompanied by abject acceptance and detachment. Two patients (cases 4 and 5) tried to conceal their suicidal feelings and impulses and to continue fluoxetine treatment, believing that the drug would eventually enable them to successfully kill themselves!

A great deal has been written on the possible role of serotonin in violence, suicide, and obsessive behavior (4–7), and fluoxetine is known to be a potent and selective serotonergic uptake inhibitor (8, 9). Given this background, we were especially surprised to witness the emergence of intense, obsessive, and violent suicidal thoughts in these patients. Their suicidal thoughts appear to have been obsessive, as they were recurrent, persistent, and intrusive. They emerged without reason but were the patients' own thoughts. It was also remarkable how violent these thoughts were. Two patients fantasized, for the first time, about killing themselves with a gun (cases 4 and 5), and one patient (case 6) actually placed a loaded gun to her head. One patient (case 2) needed to be mained the same, and patient 5 may have had a slight initial antidepressant response. Patients 2 and 4 are presently free from active suicidal ideation even though they are depressed, and all of these patients had been depressed previously but had never been so violently suicidal. Second, it is possible that suicidal thoughts emerged for reasons unrelated to fluoxetine treatment (e.g., loss or abandonment), although no evidence could be found to support this alternative. In fact, no patient was able to articulate a reason for feeling so suicidal. Third, it is possible that other pharmacological factors or interactions may have been involved. Most patients were receiving treatment with other drugs that could have also contributed to this response, although they were free from active suicidal thoughts while taking these drugs before fluoxetine treatment. Fluoxetine can markedly alter the metabolism of concomitantly administered medications (8), and drug interactions may be an important factor. Similarly, their previous histories of treatment with tricyclic antidepressants, MAOIs, or neuroleptics may be relevant risk factors.

There is no simple explanation of why these patients seemed to react so adversely to fluoxetine. It is noteworthy that they all had hypersomnia, fatigue, or psychomotor retardation before or during treatment with fluoxetine. Four patients also complained of a disturbing sense of inner restlessness, and they may have had a form of akathisia (cases 1–3 and 6), which could be a contributing factor. None of the patients had a prominent therapeutic response to fluoxetine, and we have not observed the emergence of suicidal ideation in any patient who was clearly benefiting from this drug.

At the present time we can only state that persistent, obsessive, and violent suicidal thoughts emerged in a small minority of patients treated with fluoxetine. Fluoxetine was the sole pharmacologic agent in only two cases; the other patients were taking a variety of other medications, which may have also contributed to this reaction and thereby complicate interpretation. The purpose of this report is to suggest the surprising possibility that fluoxetine may induce suicidal ideation in some patients. Only additional surveillance will enable us to learn whether this is a widespread or valid concern. In our own experience, this side effect has occurred in 3.5% of patients receiving fluoxetine, which provides an estimated incidence of 1.3%–7.5% with 95% confidence limits. Clinicians should be alert to this possibility and should query patients carefully about suicidal ideation, particularly if they are not responding well to treatment. Recently we have started to inform patients of this risk and have told them that this medication does not always work, that some patients feel worse, and that a few have developed suicidal thoughts. They are instructed to call if they develop side effects or start to feel worse.

At the present time we recommend that this drug be used cautiously and that the practitioner be attentive to the possible emergence of suicidal ideation, even in those patients without a previous history of suicidal thoughts or actions. Patients who have previously been treated with other antidepressants or who develop intense fatigue, hypersomnia, or restlessness while taking fluoxetine may be at risk.

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# Chronicity and a Low Anteroposterior Gradient of Cerebral Blood Flow in Schizophrenia

Roy J. Mathew, M.D., and William H. Wilson, Ph.D.

*Regional cerebral blood flow (CBF) was measured with the $^{133}$xenon inhalation technique in 27 patients with schizophrenia of less than 5 years' duration and in 27 patients with schizophrenia of more than 12 years' duration, under resting conditions. Similar measurements were also performed in 54 normal control subjects matched for age and sex. Patients with schizophrenia of long duration had lower anteroposterior gradients of CBF than patients with schizophrenia of short duration and matched control subjects. Covarying out age and end-tidal levels of $CO_2$ did not alter the results.*

(Am J Psychiatry 1990; 147:211–213)

A low anteroposterior gradient in cerebral blood flow (CBF) distribution in schizophrenia is a topic of considerable research interest (1, 2). Initial reports of a low anteroposterior gradient by Ingvar and Franzen (3, 4) were confirmed by several investigators with both two-dimensional and three-dimensional CBF measurement techniques. However, several others could not replicate this finding (1, 2). Although the exact reasons for the discrepancy are unclear, chronicity of schizophrenia would seem to be an important factor.

In the report by Ingvar and Franzen, anteroposterior gradient reduction was most marked in patients with schizophrenia of long duration (3, 4). Similar findings were also reported by Mubrin and associates (5). In a recent study conducted in our laboratory, in which 107 patients with schizophrenia participated, the only clinical variable related to the low anteroposterior gradient was duration of the illness (1). To examine the issue of anteroposterior gradient in greater detail, we selected two subgroups of patients with schizophrenia who differed substantially in duration of illness and compared them with two age- and sex-matched control groups.

## METHOD

Fifty-four medicated patients with schizophrenia—27 patients with duration of illness of less than 5 years (short-duration patients) and 27 patients with duration of illness of more than 12 years (long-duration patients)—participated in the study. The Schedule for Affective Disorders and Schizophrenia (6) was used to establish the diagnosis on the basis of *DSM-III-R* criteria. All participants were hospitalized at the time of the study; the diagnostic subtypes were subchronic with acute exacerbation and chronic with acute exacerbation. None of the patients were in remission, and none met the criteria for residual type. Duration of schizophrenia for the two groups is shown in table 1. The number of previous hospitalizations for short-duration patients and long-duration patients was 3.0±1.6 and 6.8±4.0, respectively. Both groups of patients were receiving antipsychotic drugs at the time of the study; the two groups did not differ on doses when they were converted to chlorpromazine equivalents (7). Physical examination and hematological and biochemical laboratory tests were used to exclude patients with significant physical illnesses. Written informed consent was obtained from all patients.

Two groups of control subjects, matched for age and sex with the two patient groups, were selected from normal volunteers. They were medication free and physically and mentally healthy. All subjects avoided caffeine and tobacco (8) for 2 hours before the CBF measurements.

CBF measurements were performed with the $^{133}$xenon inhalation technique (9). In this technique, $^{133}$xenon mixed with room air (5–7 mCi/liter) is administered to the patient through a face mask for 1 minute. Gray matter perfusion rates are computed from the rate at which the isotope is cleared from the brain; these rates are monitored by a system of 32 scintillation detectors mounted on a helmet and applied to the scalp. Details of the technique, laboratory procedures, and routine precautions are described elsewhere (1). $CO_2$ is a potent cerebral vasodilator (10, 11), and end-tidal levels of $CO_2$ ($Pe_{CO_2}$) were monitored during the CBF measurements. All measurements were performed while the patients were in a quiet, semidark room with their eyes open.

The CBF values were computed separately for each

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**TABLE 1. Clinical Characteristics of Patients With Long- and Short-Duration Schizophrenia and of Age- and Sex-Matched Normal Control Subjects**

| Group | N | Age (years)[a] Mean | Age (years)[a] SD | Sex M | Sex F | Length of Illness (years)[b] Mean | Length of Illness (years)[b] SD | $Pe_{CO_2}$ (mm Hg) Mean | $Pe_{CO_2}$ (mm Hg) SD |
|---|---|---|---|---|---|---|---|---|---|
| Patients | | | | | | | | | |
| Long-duration | 27 | 41.8 | 10.4 | 11 | 16 | 21.6 | 8.5 | 36.6 | 3.8 |
| Short-duration | 27 | 31.4 | 12.8 | 17 | 10 | 2.4 | 1.7 | 37.5 | 4.1 |
| Control subjects | | | | | | | | | |
| Matched with long-duration patients | 27 | 41.5 | 11.4 | 11 | 16 | — | — | 38.0 | 4.8 |
| Matched with short-duration patients | 27 | 32.4 | 13.9 | 17 | 10 | — | — | 36.7 | 4.1 |

[a] The long-duration patients and control subjects were significantly older than the short-duration patients and control subjects (F=17.07, df=1, 104, p≤0.001).

[b] Significant difference between the two patient groups (t=11.47, df=24, p≤0.001, two-tailed test).

of the 32 individual detector channels. The anteroposterior gradient in CBF for each hemisphere was calculated by dividing the mean value for the precentral detector channels (five frontal, two central) by the mean value for the postcentral detector channels (three temporal, four parietal, and two occipital) and multiplying this ratio by 100. This approach was used in a previous report from this laboratory on CBF in schizophrenia (1).

## RESULTS

There were no differences between the patient groups and their corresponding control groups on age, but the long-duration patients and control subjects were significantly older than the short-duration patients and control subjects (table 1). Analyses of physiological variables revealed slight but statistically significant higher pulse and respiration rates in patients than in control subjects but no difference between patient groups. There were no differences in $Pe_{CO_2}$ among the four groups (table 1).

Because of the age difference the short- and long-duration patients (and consequently their control subjects), analyses of CBF were carried out with two approaches: 1) by using age as a covariate and 2) by separately comparing patients with their respective age- and sex-matched control subjects. Analyses of the anteroposterior gradient (by using a Diagnosis by Duration model, with age covaried) indicated main effects for diagnosis (patients had a significantly lower anteroposterior gradient than control subjects [F=6.04, df=1, 103, p≤0.02]), and there was a main effect of duration (F=5.46, df=1, 103, p≤0.02). Comparison between the two patient groups, with age covaried, indicated a significant difference (F=5.98, df=1, 52, p≤0.02), with patients with long duration of illness having lower anteroposterior ratios, but a similar comparison between the control groups found no difference.

When the patients were compared with their control subjects, short-duration patients did not differ from their control subjects, even when age and $Pe_{CO_2}$ were covaried. However, long-duration patients had a significantly lower anteroposterior ratio than their control subjects (p≤0.01, Scheffé test). This result became more statistically significant when age and $Pe_{CO_2}$ were covaried out of the model (F=7.69, df=1, 50, p≤ 0.008). $Pe_{CO_2}$ was covaried in spite of the absence of statistically significant differences between the groups because of its extremely strong effect on CBF (10, 11). There was no interhemispheric difference in the anteroposterior gradient (figure 1).

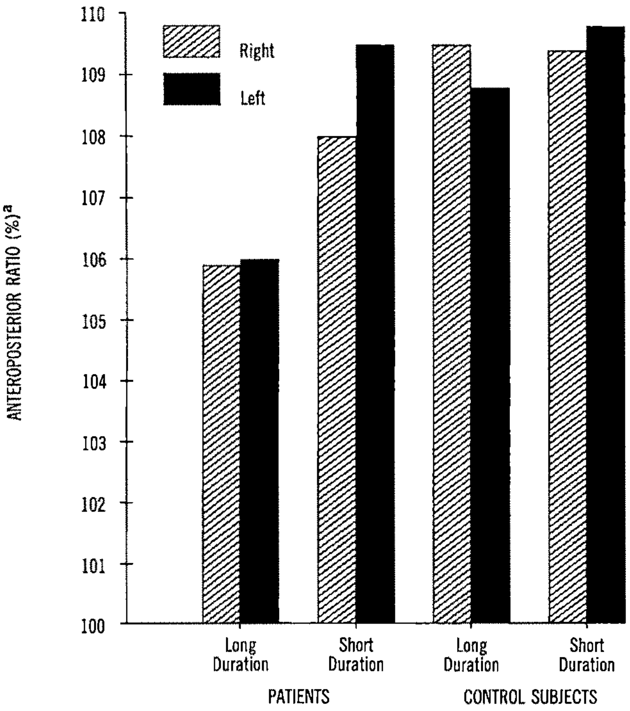
## DISCUSSION

The results of the present study indicate that a lower anteroposterior gradient is, at least in part, a function of chronicity of schizophrenia. Patients with schizophrenia of long duration showed a significantly lower anteroposterior gradient of CBF than patients with short-duration schizophrenia and age- and sex-matched control subjects. Short-duration patients did not differ from matched control subjects on the anteroposterior gradient. The most significant low anteroposterior gradients, reported by Ingvar and Franzen (3, 4) as well as by Mubrin and associates (5), were in older patients (ages: mean=61 years, range=49–72, and mean±SD= 38.4±6.2, respectively).

Patients who have been sick longer are also likely to be older. Normal aging has been found to be associated with reduced frontal blood flow and lower anteroposterior gradient (11). Thus, the effect of age-related CBF changes needs to be considered in studies of CBF in patients with schizophrenia of long duration.

The results of the present study indicate that the lower anteroposterior gradient in schizophrenia of long duration cannot be explained on the basis of age-related changes. The patients with long-duration schizophrenia were considerably younger (mean±SD age= 41.8±10.4 years) than the "older" patients studied by

**FIGURE 1. Anteroposterior Ratios of Regional Cerebral Blood Flow in Patients With Long- and Short-Duration Schizophrenia and Age- and Sex-Matched Normal Control Subjects**



[a]The standard deviations for the right and left anteroposterior ratios are as follows: long-duration patients, 5.5 and 4.6, respectively; short-duration patients, 4.0 and 6.2; long-duration control subjects, 4.7 and 4.7; and short-duration control subjects, 5.2 and 5.3.

Ingvar and Franzen (3, 4) but were comparable in age to Mubrin and associates' patients (5). Thus, age-related CBF changes were likely to be milder in the patients with schizophrenia of long duration who took part in our study and the study by Mubrin and associates. In our study, long-duration patients showed a significantly lower anteroposterior gradient than short-duration patients and age- and sex-matched control subjects. Covarying out age did not alter the results. In an earlier study we reported an anteroposterior gradient difference between normal men and women (11). In the present study, although there was a nonsignificant difference between the two patient groups in the male:female ratio, patients and control subjects were matched on sex. Thus, in the present study, low anteroposterior gradient in patients with schizophrenia of long duration could not be explained on the basis of age, gender, or $Pe_{CO_2}$. Long- and short-duration patients were receiving comparable doses of antipsychotic medication, and therefore the difference in anteroposterior gradient cannot be due to the immediate effect of drugs. Long-duration patients might have been receiving these drugs for a longer period of time, however. The effect of long-term exposure to antipsychotic medication on CBF is unclear.

The low anteroposterior gradient may be specifically related to symptoms associated with long-duration schizophrenia, such as indifference and inactivity, which may be linked to low frontal blood flow (3, 4). These symptoms were not quantified in the present study, and therefore the effect of symptoms of CBF could not be evaluated. Low frontal blood flow has been reported in a variety of conditions including normal aging (11), primary degenerative dementia (12), chronic alcoholism (13), long-term exposure to organic solvents (14), and depression (15). Frontal blood flow may also be sensitive to sensory and cognitive activation (16). Thus, it is unclear whether the low anteroposterior gradient in chronic schizophrenia is an epiphenomenon or a specific characteristic of the syndrome.

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# Frequency and Correlates of Childhood Sexual and Physical Abuse Histories in Adult Female Borderline Inpatients

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*Suspected complex partial seizure disorder, eating disorders, and drug abuse disorders were overrepresented among the 40% (N=16) of female borderline inpatients who reported a history of sexual abuse. Early family disruption, more frequent hospital admissions, and concomitant antisocial personality disorder were overrepresented among those who reported past physical abuse.*

(Am J Psychiatry 1990; 147:214–216)

Numerous reports suggest a high prevalence of childhood sexual or physical abuse in the histories of adult patients with significant psychiatric or substance abuse disorders. The diagnosis of borderline personality disorder is particularly prevalent among adult patients with a history of such developmental traumas (1).

Many of the reported long-term consequences of childhood sexual abuse are identical to *DSM-III-R* criteria for borderline personality disorder. That is, patients with childhood sexual abuse and borderline personality disorder frequently display impulsivity, self-destructive behavior, substance abuse, identity disturbance, and chronic dysphoria. The greater vulnerability of female children to sexual abuse has been linked to the disproportionate number of women assigned the borderline diagnosis (1).

Small-sample pilot data have suggested that the prevalence of childhood sexual abuse in adult women with a diagnosis of borderline personality disorder ranges from 67% to 86% (1). Reported histories of physical abuse in mixed sex samples of borderline patients range from 46% (2) to 71% (1). Although the borderline diagnosis is more prevalent in groups of abused psychiatric patients than in unabused patients (1, 2), it is not clear how abused borderline patients may differ from unabused ones.

The literature in this area has not yet clarified whether different abusive experiences in childhood contribute to different residual effects in adulthood. For example, incest was reported to have a worse impact than other forms of childhood sexual abuse in a nonclinical population (3) but an equivalent effect in a clinical population (4). Herman and her colleagues (5) have reported that abuse by a parental figure, forceful violation, and prolonged victimization were associated with more severe sequelae. Childhood physical abuse has received less attention in this literature and has often been grouped with sexual abuse; however, at least one study has suggested that the additive consequences of physical and sexual abuse are more adverse than either alone (4).

The present study examined the frequency and significant correlates of self-reported childhood abuse histories in a sample of adult female borderline inpatients.

## METHOD

This study was conducted as an adjunct to a primary investigation of suicidal behavior among female psychiatric inpatients with a diagnosis of borderline personality disorder. The methodology and demographic description of subjects for that study have already been published (6) and will not be reiterated here. This study included the same measures and the same 40 patients but focused on variables of childhood abuse assessed by semistructured interview.

A history of childhood sexual abuse was defined as any sexual contact with a nonpeer (i.e., 5 years senior) before age 15 years. A history of incest was defined as any sexual contact with a relative or parental figure (e.g., stepfather) before age 15 years. A history of physical abuse was defined as physical abuse, with physical injury, by a parental figure on more than one occasion before age 15 years.

The preponderance of dichotomous variables, small sample size, nonindependent subgroups, and numer-

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**TABLE 1. Abuse Before Age 15 Reported by 40 Adult Female Inpatients With Borderline Personality Disorder**

| Category of Abuse | N | Relevant Variables | Significance[a] |
|---|---|---|---|
| Any reported sexual abuse by a non-peer | 16 | Documented/suspected complex partial seizure disorder[b] | $p=0.01$ |
| | | Eating disorder[c] | $\chi^2=4.17$, df=1, $p=0.04$ |
| | | Drug abuse disorder[d] | $p=0.05$ |
| Incest | 11 | Documented/suspected complex partial seizure disorder | $p=0.001$ |
| Physical abuse with injury | 10 | Early familial disruption[e] | $p=0.02$ |
| | | Number of psychiatric hospital admissions | $p=0.03$ |
| | | Concomitant antisocial personality disorder[f] | $p=0.03$ |
| "Worst" abuse | 7 | Documented/suspected complex partial seizure disorder | $p=0.007$ |
| | | Early familial disruption | $p=0.01$ |

[a] Fisher's exact test, two-tailed, unless otherwise specified.

[b] N=7; includes three patients with documented EEG temporal focus and four patients in whom complex partial seizure disorder was clinically suspected but not clearly corroborated by EEG findings.

[c] N=16; includes bulimia (N=8), anorexia nervosa (N=2), eating disorder mixed (N=5), and atypical eating disorder (N=1).

[d] Diagnosis based on the Schedule for Affective Disorders and Schizophrenia—Lifetime Version.

[e] Defined as preadolescent loss of parent by death, divorce, or extended physical separation.

[f] Diagnosis based on the Personality Disorder Examination—First Revision.

ous comparisons are relevant statistical concerns. Continuous variables were converted into dichotomies, for statistical analyses, according to whether a given score fell above or below the median. The characteristics of borderline patients who either reported or denied various abuse experiences were then compared on 60 variables by using Yates'-corrected chi-square analyses. The Fisher's exact test was used in all instances in which the expected frequency for any cell was below five.

## RESULTS

The frequency of various abuse experiences, relevant variables, and statistical significance levels are reported in table 1. Borderline patients who reported a history of any sexual abuse were significantly more likely to have a concomitant diagnosis of suspected complex partial seizure disorder, an eating disorder, or a drug abuse disorder. A reported history of incest was significantly associated only with suspected complex partial seizure disorder. Statistical trends suggested a relationship between incest and lethality of self-destructive behavior, age when first hospitalized, psychotic symptoms, and eating disorders.

A reported history of physical abuse was significantly associated with early family disruption, a greater number of psychiatric hospital admissions, and a concomitant axis II diagnosis of antisocial personality disorder. Statistical trends suggested a relationship between physical abuse and a history of psychotic symptoms and somatization. Combination of antisocial personality disorder or somatization disorder into a "primary character disorder" (7) variable yielded a relationship with a history of physical abuse ($p=0.001$, Fisher's exact test, two-tailed).

A "worst abuse" category was formed by subjective selection of seven patients who were the victims of particularly severe abuse, according to types of abuse, duration, or multiple perpetrators. This worst abuse variable was significantly associated with suspected complex partial seizure disorder and with a history of early family disruption.

## DISCUSSION

Several clinically relevant variables associated with histories of childhood abuse were identified in a sample of 40 female inpatients with borderline personality disorder. The small sample, the lack of independence among compared subgroups, and use of only dichotomous data that obscure much individual variability all temper interpretation of these findings.

The most striking finding was the repeated appearance of probable complex partial seizure disorder as a relevant variable. This subgroup is, admittedly, small and poorly defined; only three of seven patients had EEG abnormalities sufficient to corroborate the treatment team's clinical impression. We included this variable in the original study (6) only because we wondered if it might represent a disinhibiting factor for more serious self-destructive behavior, and we were surprised by its repeated appearance among sexual abuse data, particularly incest. This finding seems unlikely to represent merely the residual effect of abuse-caused physical injuries, since the seizure disorder was associated only with sexual abuse, rather than physical abuse. One hypothesis is that these were neurologically compromised children whose deficits may have contributed to the formation of inappropriate relationships in susceptible families (8). Another hypothesis is that dissociative symptoms, commonly associated with childhood trauma, were mistaken as clinical evidence of complex partial seizure disorder. Alternatively, perhaps repetitive traumatic experiences could actually "kindle" limbic system alterations, eventually manifested in adulthood as some combination of complex partial seizure disorder and chronic posttraumatic stress disorder. Such a hypothesis is consistent both with recent theoretical formulations about kindling and the concept of "disorders of arousal" (9) and with preliminary empirical applications, such as the use of carbamazepine in posttraumatic stress disorder (10). This intriguing finding requires replication in a larger sample, with more stringent definition of CNS dysfunction.

Although etiology cannot be inferred from correlations, the growing literature in this area certainly provokes reassessment of traditional etiological hypotheses about borderline personality disorder. We do not propose a simplistic model of abuse as a singular cause of borderline personality disorder. Abuse usually occurs in the context of other family problems, including parental alcoholism or affective disorder, physical impairment or death of a parent, and fragmentation of the family. Hence, abuse victims are also burdened with the legacy of genetic predisposition or multiple developmental traumas, which compound the specific effects of victimization. Abuse experiences may nonetheless prove to be characteristic of a significant subgroup of borderline patients; this group may be typified particularly by features of complex partial seizure disorder and posttraumatic stress disorder suggestive of underlying alterations in limbic system functioning. Psychotherapeutic and psychopharmacologic interventions specific to this subgroup may evolve from such findings.

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# Anxiety Disorders in Patients With Parkinson's Disease

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*To study the prevalence and importance of anxiety disorders in patients with idiopathic Parkinson's disease, the authors systematically evaluated 24 parkinsonian patients for the presence of* DSM-III-R *axis I syndromes. Nine subjects (38%) had a clinically significant current anxiety disorder. Severity of anxiety was not correlated with severity of parkinsonian symptoms, cumulative duration of* L*-dopa exposure, or current dose of* L*-dopa. These findings suggest that anxiety disorders should be considered in the medical evaluation and treatment of parkinsonian patients and that further attention should be paid to the role of the dopaminergic system in anxiety and phobic disorders.*
(Am J Psychiatry 1990; 147:217–220)

Parkinson's disease and its treatment are associated with considerable psychiatric morbidity. Patients with Parkinson's disease are at increased risk for the development of depression (1–4) and dementia (5). In addition, medications used to treat Parkinson's disease—particularly drugs that facilitate dopaminergic neurotransmission, such as L-dopa, amantadine, and bromocriptine—may cause a variety of neuropsychiatric side effects, including psychosis and delirium (6, 7).

Recently, our clinical observations have suggested to us that patients with Parkinson's disease experience many symptoms of anxiety, including panic attacks. Our clinical impression has been that these symptoms are quite prevalent and may contribute to the overall disability experienced by patients with Parkinson's disease. Furthermore, we have observed that some patients with the "on-off" phenomenon (8), a phasic fluctuation in parkinsonian motor symptoms consisting of alternating dyskinetic and akinetic periods, complained of intense autonomic symptoms (e.g., tachycardia, sweating) and fear as they were entering an off phase. We speculated that these episodes might be related to panic attacks and might, therefore, teach us something about the pathophysiology of panic disorder. We sought to test these hypotheses in an unselected sample of Parkinson's disease patients by systematically evaluating the presence and prominence of specific anxiety disorders and their relationship to various aspects of the Parkinson's disease process.

## METHOD

We studied 24 patients (five women and 19 men) who had idiopathic Parkinson's disease without dementia (Mini-Mental State [9] scores$\geq$27). The mean$\pm$SD age was 58.3$\pm$8.8 years (range=31–70 years).

All patients gave informed consent before participating in the study. The patients were assessed by a research psychiatrist (M.B.S.) with a semistructured diagnostic interview derived from the Schedule for Affective Disorders and Schizophrenia—Lifetime Version Modified for the Study of Anxiety Disorders (10), and *DSM-III-R* axis I diagnoses were applied. Adhering strictly to *DSM-III-R* hierarchical rules and exclusion criteria, we divided the patients into a group with and a group without anxiety disorders. Additionally, we required that the disorder cause either moderate or severe occupational or social impairment in order to be designated as an anxiety disorder for the purposes of this study. The patient's degree of anxiety and panic symptoms were rated using the Sheehan Clinician-Rated Anxiety Scale (11). For each patient we determined which symptoms on the Sheehan scale were clearly secondary to the physical effects of Parkinson's disease, and these were subtracted from the total score to yield an adjusted Sheehan anxiety score for the patient.

A research neurologist (I.J.H.), who did not know the patient's specific *DSM-III-R* diagnosis, recorded each patient's historical and medication data and determined the current stage of his or her parkinsonism with the Hoehn and Yahr scale for motor disability (12), a 5-point scale that is commonly used to measure the stages of Parkinson's disease. The neurologist also documented each patient's type of response to L-dopa: 1) never treated with L-dopa, 2) stable response, 3) wearing-off fluctuations, or 4) on-off fluctuations (8). The same examiner, experienced in the use of the Zung

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**TABLE 1. Clinical Data on 24 Parkinson's Disease Patients With and Without Anxiety Disorders**

| | Patients Without Anxiety Disorders (N=15) | | Patients With Anxiety Disorders (N=9) | | | | |
|---|---|---|---|---|---|---|---|
| Item | Mean | SD | Mean | SD | t | df | p |
| Age (years) | 60.7 | 6.3 | 54.3 | 11.2 | 1.80 | 22 | 0.09 |
| Age at onset (years) | 48.1 | 8.1 | 46.7 | 9.6 | 0.38 | 22 | n.s. |
| Duration of illness (years) | 12.7 | 6.7 | 7.7 | 5.1 | 1.92 | 22 | 0.07 |
| Cumulative L-dopa exposure (years) | 8.4 | 6.2 | 5.8 | 5.5 | 1.01 | 22 | n.s. |
| Current L-dopa dose (mg/day) | 867 | 535 | 811 | 788 | 0.21 | 22 | n.s. |
| Sheehan anxiety score | | | | | | | |
| Total[a] | 17.4 | 10.8 | 35.0 | 22.4 | — | — | — |
| Adjusted[b] | 10.6 | 8.5 | 28.2 | 17.5 | — | — | — |
| Hamilton depression score | 12.0 | 10.2 | 17.4 | 9.2 | 1.20 | 18 | n.s. |
| Zung anxiety score | 40.9 | 10.1 | 47.4 | 15.7 | 1.13 | 18 | n.s. |
| Hoehn and Yahr motor disability score | 2.9 | 1.2 | 2.7 | 1.4 | 0.49 | 22 | n.s. |

[a] Mann-Whitney U=33, N=21, p=0.06.
[b] Mann-Whitney U=24, N=21, p=0.01.

Anxiety Scale (13) and the Hamilton Rating Scale for Depression (14), rated each patient's symptoms on these two scales.

Patients with anxiety disorders (N=9) were compared to those without anxiety disorders (N=15) across all variables by means of Student's t test (two-tailed) or the Mann-Whitney U test (two-tailed). The prevalence of anxiety disorders in patients with on-off fluctuations in parkinsonian symptoms was compared to that in patients without on-off fluctuations by means of a one-tailed chi-square test, in order to test our hypothesis that patients with on-off fluctuations would have more anxiety disorders. All data are expressed as mean±SD. All p values≥0.10 were considered nonsignificant; p values<0.10 are specifically reported.

## RESULTS

Nine (38%) of the 24 patients with Parkinson's disease received a *DSM-III-R* diagnosis of current anxiety disorder. Of these nine patients, one had generalized anxiety disorder, two had panic disorder (with or without agoraphobia), one had long-standing panic disorder with the recent onset of a superimposed major depressive episode, one had panic disorder and social phobia, three had social phobia alone, and one had an anxiety disorder not otherwise specified. Three additional subjects had clinically significant social anxiety, but their anxiety was judged to be secondary to their self-consciousness and embarrassment about their parkinsonian symptoms being visible to others. This is listed as an exclusion criterion for the diagnosis of social phobia in *DSM-III-R*, so these three subjects were excluded from the subgroup of patients with formal *DSM-III-R* anxiety disorders. Nonetheless, we wish to emphasize that a total of seven (29%) of the parkinsonian patients suffered from clinically significant social phobic symptoms.

Of the nine subjects with formal *DSM-III-R* anxiety disorders, two (22%) had the onset of the anxiety disorder before the diagnosis of Parkinson's disease, and seven (78%) had the onset of the anxiety disorder after the diagnosis of Parkinson's disease. In addition to the subjects with anxiety disorders, two other subjects had mood disorders (one had hypomania and one had major depression). Ten subjects had no current psychiatric diagnosis.

The nine patients with significant anxiety disorders and the 15 without significant anxiety disorders were compared across all salient variables (table 1). There was a trend (p values<0.10) for the patients with anxiety disorders to be younger and to have been ill with Parkinson's disease for a shorter period of time. There were no significant differences between the two groups in cumulative duration of L-dopa exposure, current L-dopa dose, or degree of motor disability (Hoehn and Yahr scale). Patients with anxiety disorders had higher total and adjusted scores on the Sheehan anxiety scale, higher Hamilton depression scores, and higher Zung anxiety scores, although the differences reached a level of statistical significance only for the Sheehan adjusted scores.

We observed no significant relationship between the on-off pattern and the presence or absence of anxiety disorders when we compared the patients with on-off fluctuation (N=6) and those without on-off fluctuations (N=18). Nonetheless, we identified one patient who, in longitudinal follow-up, consistently experienced panic attacks when entering an off phase, which suggests that there may be a relationship between mo-

**TABLE 2. Lifetime Prevalence of Psychiatric Disorders in Patients With Parkinson's Disease, Patients With Other Chronic Medical Illnesses, and the General Population**

| | Percent of Subjects | | | | |
|---|---|---|---|---|---|
| Disorder | Patients With Parkinson's Disease (N=24) | Patients With Multiple Sclerosis (Joffe et al. [15]) (N=100) | Patients With Type I Diabetes Mellitus (Popkin et al. [16]) (N=75) | Patients With Rheumatoid Arthritis (Kirmayer et al. [17]) (N=23) | General Population (Robins et al. [18]) (N=9,543) |
| Panic disorder | 21 | 5 | 1 | 5 | 1 |
| Social phobia | 17 | — | 7 | — | 2[a] |
| Obsessive-compulsive disorder | 0 | — | 1 | 4 | 3 |
| Generalized anxiety disorder | 4 | 3 | 32 | — | — |
| Major depression | 46 | 47 | 24 | 9 | 5 |
| Schizophrenia | 0 | 0 | — | — | 2 |

[a] Data from Pollard and Henderson (19).

toric and anxiety symptoms in at least a subgroup of patients with Parkinson's disease.

Table 2 shows the lifetime prevalence of psychiatric syndromes in the 24 patients with Parkinson's disease and rates from similar studies of patients with several other chronic medical illnesses (15–17) and of the general population (18, 19). While these comparisons should be viewed only as first approximations pending further direct comparison in future controlled studies, there is some evidence to suggest that Parkinson's disease patients exhibit higher than expected rates of panic disorder and social phobia.

## DISCUSSION

We found that nine (38%) of 24 patients with Parkinson's disease had a clinically significant anxiety disorder at the time of evaluation. This compares with estimates of 5%–15% for anxiety disorders in the general population (20), less than 10% in patients in a primary care clinic (21), and approximately 11% in patients with chronic medical conditions (22). As shown in table 2, the lifetime prevalence of panic disorder and social phobia in these 24 patients also appears to be higher than that in patients with multiple sclerosis (15), type I diabetes mellitus (16), and rheumatoid arthritis (17). Our findings therefore suggest that the occurrence of anxiety disorders may be a relatively neglected subject in the literature on neuropsychiatric problems in Parkinson's disease. The theory that there is a higher rate of anxiety disorders in patients with Parkinson's disease is further supported by a recent study (23) that found more frequent panic and anxiety symptoms in 16 depressed patients with Parkinson's disease than in 20 depressed patients with multiple sclerosis.

There are at least three viable explanations (none of which excludes the others) for why anxiety disorders, as well as depressive disorders, seem to be more prevalent in patients with Parkinson's disease and other chronic disease states. First, the psychiatric disturbance might be a psychological response to having a chronic disease and the impairment resulting from the disorder. Although this explanation remains controversial, most studies suggest that depression in Parkinson's disease is not merely a byproduct of living with a chronic, disabling illness (2–4, 24, 25). Our findings regarding anxiety disorders are similar: the group of subjects with significant anxiety disorders was no more severely disabled than the group without significant anxiety disorders, nor had they been ill for a longer period of time. Certainly, the psychological impact of Parkinson's disease and its effect on lifestyle should not be overlooked, but this seems to be an incomplete explanation for our findings.

A second explanation is that the psychiatric disturbance might be a function of medication treatment. The acute neuropsychiatric side effects of L-dopa are legion (6), and long-term use of L-dopa has been associated with the development of increased motor fluctuations (specifically, the on-off phenomenon [8]). Nonetheless, we did not find higher current L-dopa doses or longer duration of L-dopa treatment in the group with anxiety disorders. However, because many subjects were taking other antiparkinsonian drugs such as anticholinergics, amantadine, and bromocriptine, we cannot exclude the potential influence of these drugs.

A third explanation for the seemingly higher prevalence of anxiety disorders in patients with Parkinson's disease is that the psychiatric disturbance might be a function of some common pathophysiologic process. It appears probable (although this remains controversial) that a dopaminergic deficit in Parkinson's disease may exist not only in the striatum, accounting for motor symptoms, but also in the mesolimbic and mesocortical areas of the brain (26), perhaps thereby contributing to psychiatric symptoms. Liebowitz et al. (27) have proposed that social phobia may involve dopaminergic dysregulation and that dopamine agonists may prove useful in the treatment of this disorder. In one study of depressed patients (28), CSF dopamine levels were correlated with the psychological dimension of extroversion. Conceivably, the dopaminergic deficit experienced by parkinsonian patients could contribute to a lack of extroversion, phenomenologically expressed as social phobia. Furthermore, two recent studies from our Section on Anxiety and Affective Disorders found that patients with panic disorder may have abnormal plasma levels of the dopamine metabolite homovanillic acid (29, 30). These data suggest that the dopaminergic system may indeed play a role in the pathogenesis of anxiety disorders, although considerable further research will be needed to define discrete mechanisms. Our finding of a high rate of anxiety disorders in a group of patients with definite dopaminergic dysfunction (Parkinson's disease) should serve as an impetus to further study in this area.

In conclusion, our preliminary findings raise more questions than they can answer. It remains to be seen from future controlled studies in nonresearch settings whether the rate of anxiety disorders is genuinely higher in Parkinson's disease than in other chronic medical conditions. Nevertheless, theoretical issues aside, our observations and those of others (31) suggest that anxiety disorders may contribute to the overall morbidity experienced by patients with Parkinson's disease. Our treatment experience, not detailed here, also suggests that anxiety disorders in these patients may respond in a most gratifying manner to pharmacotherapy with antidepressants or benzodiazepines. A community study in which 11% of 841 persons with chronic medical illness had had a recent anxiety disorder (22) led the authors of that report to propose that "providers of health care should be encouraged to recognize and treat anxiety disorders in patients with chronic disease." This message surely applies to clinicians who treat patients with Parkinson's disease.

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# Witch Doctors and Mental Illness in Mainland China: A Preliminary Study

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*This study, the first report on witch doctors in the People's Republic of China, found that most witch doctors are poorly educated peasants who perform healing rituals as a part-time occupation. Despite being officially illegal, folk healing practices are flourishing in the countryside: 73.9% (N=286 of 387) of psychiatric outpatients from rural areas and 70.5% (N=43 of 61) of mentally ill persons identified in a rural community admitted to consulting witch doctors. These findings indicate an urgent need to systematically assess the beneficial and detrimental effects of these practices on China's health care system.*

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In mainland China, most witch doctors (*Wu Yi*) are poorly educated peasants without any formal medical or religious training who do shamanistic or other types of ritual healing on a part-time basis. The official government position is that these practices are illegal. Local authorities actively prosecuted witch doctors during the 1950s and 1960s, but more recently they have tolerated witch doctors except for those whose practices cause physical injury to their patients. Witch doctors' methods are pluralistic, combining aspects of Taoist, Buddhist, and animistic beliefs (1). They explain illnesses in terms of spirits and ghosts, and they state that they treat patients by intervening in the spirit world on their behalf.

Despite the recent relaxation of controls, witch doctors usually deny the practice when interviewed because they remain fearful of official censure. Thus, it is extremely difficult to collect data about witch doctors and their practices. Moreover, Chinese medical researchers, most of whom live in large cities, are unaware of the major role that witch doctors play in the health care delivery system in the countryside. To our knowledge, there has never been any published research on witch doctors in the People's Republic of China.

Since traditional belief systems frequently attribute mental illnesses to disturbances in the spirit world, analysis of the use of witch doctors by persons with mental illnesses is an appropriate starting point for research on folk healing. Our hospital, a 550-bed psychiatric hospital in central China, is well-suited for such a study because our catchment population (Jingzhou district of Hubei province, population 11,000,000) is primarily composed of peasants.

## METHOD AND RESULTS

The first step was to assess utilization of witch doctors by persons who came to our outpatient psychiatric clinic from April 1984 thru April 1985. Of 421 randomly selected patients, 292 (69.4%) admitted to consulting witch doctors before coming to the clinic (case 1). As expected, the rate among rural patients was significantly higher than the rate among urban patients: 73.9% (N=286 of 387) versus 17.6% (N=6 of 34) ($\chi^2$=43.9, df=1, p<0.001).

Since some rural patients with mental illness may never seek psychiatric treatment, the next step was to determine utilization of witch doctors by mentally ill persons in the community. Mentally ill persons in Li-Chang county, a typical rural county in Jingzhou district (population 34,758), were located by asking three types of key informants (previously treated psychiatric patients, local medical workers, and local leaders) to identify persons that they felt had any kind of psychological problem. Using a Chinese diagnostic screening instrument (2), the first author found that 61 of the 84 identified subjects (including six patients previously treated in our hospital) had some type of mental disorder. The diagnoses and care-seeking behavior of these 61 persons are presented in table 1. Persons with a Chinese diagnosis of hysteria (see footnote in table 1) were more likely than persons with other diagnoses to limit their care-seeking to witch doctors: 56.3% (N=9 of 16) versus 15.6% (N=7 of 45) (p<0.003, Fisher's two-tailed exact test). A total of 70.5% (N=43 of 61) of the mentally ill persons identified in the community had consulted witch doctors at some point in the course of their illness.

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**TABLE 1. Diagnoses and Care-Seeking Behavior Reported by 61 Mentally Ill Persons in LiChang County, China**

| Care-Seeking Behavior | Total |  | Schizophrenia (N=15) |  | Manic or Depressive Illness (N=10) |  | Hysteria (N=16)[a] |  | Other (N=20)[b] |  |
|---|---|---|---|---|---|---|---|---|---|---|
|  | N | % | N | % | N | % | N | % | N | % |
| Unwilling to report | 5 | 8.2 | 2 | 13.3 | 1 | 10.0 | 1 | 6.3 | 1 | 5.0 |
| Saw only regular doctor[c] | 13 | 21.3 | 6 | 40.0 | 2 | 20.0 | 0 | 0.0 | 5 | 25.0 |
| Saw only witch doctor | 16 | 26.3 | 1 | 6.6 | 1 | 10.0 | 9 | 56.3 | 5 | 25.0 |
| Saw both regular and witch doctors | 27 | 44.3 | 6 | 40.0 | 6 | 60.0 | 6 | 37.5 | 9 | 45.0 |

[a] Includes *DSM-III-R* diagnoses of brief reactive psychosis (N=6), somatoform pain disorder (N=2), depersonalization disorder (N=2), dissociative disorder not otherwise specified (N=2), and body dysmorphic disorder (N=1) and no *DSM-III-R* diagnosis (N=3) (they believed that they were possessed by ancestral ghosts).

[b] Includes adjustment disorder (N=3), mental retardation (N=4), epilepsy with psychiatric symptoms (N=2), delirium (N=1), and unspecified mental disorder (N=10).

[c] Doctors of Western medicine or of Chinese traditional medicine.

We also tried to estimate the number of witch doctors practicing in the countryside. Practical problems limited us to two small communities in LiChang county, where local police identified five active witch doctors in a total population of 2,039. The witch doctor:population ratio of 2.5:1,000 (exact 95% confidence interval=0.31–4.61:1,000) is a conservative estimate, since local residents said there were other witch doctors unknown to the police. The ratio for full-time doctors and nurses in the county is 1.9:1,000 (N=66 of 34,758).

Understanding the cultural context of folk healing requires a profile of its practitioners, so the final part of our study identified active witch doctors willing to be interviewed. Witch doctors were located by several methods. Three who had received criminal charges for witchcraft were identified by local officials; two were previously hospitalized psychiatric patients with diagnoses of brief reactive psychosis and schizophrenia (case 2); one was the father of a psychiatric patient (case 3); and eight were contacted by asking family members of psychiatric patients to introduce us to the witch doctor who had treated the patient.

Of the 14 witch doctors, 10 were interviewed directly and information on the other four was obtained by talking with family members. There were seven men and seven women. They were 19–86 years old (mean±SD age=51.3±16.5 years). The eight witch doctors who were willing to discuss their practices had practiced for 2 to 30 years (mean±SD=13.1±13.9 years). They were all peasants whose main livelihood was farming and animal husbandry; performing healing rituals was a part-time occupation. None had any training in Western medicine, Chinese medicine, pharmacology, psychology, or religious orders; indeed, seven (50%) were illiterate and three (21%) were semiliterate. Eleven (79%) originally apprenticed themselves to senior witch doctors to learn the techniques. Nine (64%) reported that before taking up the occupation, they had experienced severe psychosomatic symptoms (e.g., headaches, unexplained abdominal pain, dizziness, tachycardia) that were cured by other witch doctors. Five (36%) experienced possession states while performing healing rituals. It was not possible to do formal psychiatric evaluations, but eight nonpatient witch doctors personally interviewed by the first author showed no signs of active mental illness.

None of the witch doctors had practice records, so it was impossible to assess the volume and characteristics of their practices. Contrary to patients' reports, they all denied receiving payment, but most admitted to receiving "gifts" for their services. Despite the frequent opposition of family members and occasional disciplinary sanctions or criminal charges, they all intended to continue their practices because they thought they were doing good for others.

## CASE REPORTS

*Case 1.* Mr. A was an 18-year-old peasant with 6 years of education who worked as a temporary laborer at a rural factory. Without any clear precipitant, over a period of 2–3 days he stopped eating, did not sleep, smashed household goods, stated that he was one of the 10 field marshals of China, and talked to himself, reciting the names of famous leaders and movie actors. After 3 days of this behavior his family members went to a local witch doctor and explained the problem. Without seeing Mr. A, the witch doctor told the family that an important deity was not protecting Mr. A from evil spirits. The witch doctor wrote the patient's name, date of birth, time of birth, and a request to the deity to take especial care of Mr. A on a large piece of yellow ceremonial paper. He then burned the paper, mixed the ashes in a bowl of water, and instructed family members to make Mr. A drink the mixture. This treatment, however, was not effective, so family members consulted another witch doctor.

The second witch doctor came to Mr. A's home carrying a large sword and wearing a ceremonial hat and gown with multiple symbols woven into the fabric. He burned ceremonial paper and incense and then sat down and chanted incomprehensible words. He then rapidly entered a trance state in which his voice changed, and he said that he was a spirit who had come to drive out the evil ghost. He picked up the sword, walked around the room several times chanting, and then entered Mr. A's room, commanding the evil spirit to go. Mr. A argued loudly with the witch doctor, pushed him out of the room, and refused to take the proffered ritual drink (noncompliance!).

Subsequently, Mr. A's condition deteriorated rapidly; he could not recognize his family members, and he wandered outside without clothing. On the insistence of Mr. A's work foreman, 2 weeks after the onset of symptoms family members brought Mr. A to the psychiatric hospital; he was in a disorganized and dehydrated state. He was treated with chlorpromazine and ECT and was discharged after 95 days of hospitalization with the diagnosis of schizophreniform disorder.

*Case 2.* Ms. B was a 50-year-old widowed peasant. For 2 years before admission she repeatedly declared that she was the Jade Emperor (the supreme deity of Taoism) and that Zhou Yu and Cao Cao (famous historical figures) and current political leaders were her sons. She often sang and danced without reason. She occasionally threatened her children with a cleaver because she believed that they put poison in her food. On admission she proclaimed that she was a spirit and was totally uncooperative. One week after admission her condition was unchanged, but she was discharged (with a tentative diagnosis of schizophrenia) because the family could not afford hospitalization.

Ms. B's daughter stated that since her mother fell ill, older persons in the community had frequently brought ceremonial paper and incense to their home and had asked her mother to see their sick relatives. Apparently, many community residents believed that she was, indeed, a spirit or at least in communication with spirits; and so they sought her assistance in treating their relatives whom they thought were afflicted with evil spirits. Ms. B helped these supplicants because she had been told by a witch doctor that she would lose the protection of her spirit if she did not use the spirit's power to help others.

*Case 3.* Mr. C was a 58-year-old semiliterate peasant. At the age of 12 he felt that he was attacked by an unidentified spirit that attached itself to his back after he passed a haunted doorway. He was extremely frightened and stated that for the next 5 years this spirit caused him to have multiple episodes of severe tremors and hematemesis until the malady was finally cured by a witch doctor. He subsequently studied folk healing methods on his own and started treating others.

In his practice he differentiated "real" illnesses from illnesses that were caused by spirits. He did this by using an ancient method of computing the patient's exact time of birth by tapping his fingers. He said that if, while he was doing this computation, he heard a voice that stated the type of illness and what must be done for it, then it was an illness caused by spirits. For example, while he was assessing the time of birth of a woman who had had 2 days of high fever that was not helped by injections at the local hospital, an unknown male voice stated that "she collided with a spirit from a northeasterly direction so she should go in that direction and burn some brown paper in compensation." He stated that if, on the other hand, he heard no voice during his computation, then it was a "real" illness and he referred the person to a regular doctor (he referred his own son to the psychiatric hospital). He did not hear voices at other times. While the spirits were talking to him he felt like he was dreaming, and when he came out of the trance he felt like he was drunk (he did not drink heavily). During the interview he talked rapidly, appeared impatient, and was very suggestible, but no other psychological abnormalities were found.

## DISCUSSION

Several methodological problems need to be considered in evaluating these preliminary findings. The reported utilization rates are based on those who *admitted* to seeing witch doctors; the actual figures are probably higher. The rate of utilization of witch doctors by urban residents (17.6%) and the ratio of witch doctors in the community (2.5/1,000) were based on small denominators; these rates must be confirmed by larger studies. Our key informant method for identifying patients was not very intensive, and so some community patients were not located; the proportion of unidentified patients who see witch doctors, however, is probably similar to (or higher than) the reported proportion in identified patients (70.5%). Our 14 witch doctors are those who agreed to be interviewed and thus are probably not representative; this is a generic problem of research about quasilegal practices. And finally, to our knowledge this is the only study available in mainland China on this subject, so the representativeness of our findings is unknown; there is, however, no reason to believe that these practices and beliefs are more prevalent in our study population than in other rural parts of China.

Given these caveats, this study demonstrates that folk healing still exists in the People's Republic of China; indeed, it is flourishing in the countryside. Two separate data sources (i.e., psychiatric outpatients and persons with mental illnesses in the community) generated the same conclusion: Approximately 70% of rural residents in China with mental illnesses consult witch doctors. Given that 75% of China's population live in the countryside, this means that most Chinese persons with mental illnesses consult witch doctors at some point during their illness. The public health implications of this finding are tremendous. There is clearly an urgent need to collect data on this subject from other parts of the country and to assess the beneficial and detrimental effects of these practices on China's health care system.

The case reports highlight several points. Because of the serious lack of mental health personnel in the Chinese countryside (many rural residents are not even aware of the *existence* of psychiatric hospitals), families with disturbed members seek out witch doctors for assistance and often perceive disturbed behavior as the outcome of intervention by the spirit world. If the individual has prominently disturbed behavior that is unchanged by the ministrations of witch doctors, then local officials or medical personnel may become involved and recommend referral to psychiatric facilities. Many witch doctors start their practice after their successful treatment by another witch doctor; they are warned that failure to help others in this way will result in retribution from the spirit world and recurrence of their symptoms. A witch doctor's treatment methods and explanatory models are strongly influenced by personal experiences; those with better education and extensive exposure to health care workers may try to integrate their methods with the conventional health care delivery system.

This preliminary study does not systematically address many issues of interest to cross-cultural psychiatrists. Unlike the professional shamans of Taiwan (3), witch doctors in mainland China are part-time practitioners of an illegal activity; this fact and our limited resources made it impossible to collect the quality of data available on folk healers in other cultures. Future research will need to address several questions. 1) What types of problems are most commonly treated by witch doctors? 2) Do witch doctors provide effective psychosocial interventions for their clients? 3) From the perspective of orthodox psychiatry, do witch doctors have identifiable mental illnesses? 4) What are the psychosocial factors that induce an individual to become a witch doctor? 5) What are the sociocultural factors that sustain this officially illegal activity? We are currently engaged in a multicenter study that will more systematically address these issues.

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# CSF Monoamine Levels in Normal-Weight Bulimia: Evidence for Abnormal Noradrenergic Activity

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*Normal-weight bulimic patients have disturbed appetite, mood, and neuroendocrine function and often respond to antidepressants. Since these findings suggest abnormalities in brain monoaminergic pathways, the authors measured CSF monoamine concentrations in 27 normal-weight bulimic patients and 14 volunteers. Bulimic patients had a significantly lower mean CSF norepinephrine concentration. Levels of CSF 5-HIAA, the major serotonin metabolite, and CSF HVA, the major dopamine metabolite, were normal, although more frequent binge-eating in bulimic subjects was associated with a significantly lower CSF HVA level. Whether trait- or state-related, monoaminergic disturbances are part of this disorder's neurobiological syndrome. The lower CSF norepinephrine concentration suggests bulimia is not simply a variant of affective disorders.*

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Eating disorders have been recognized with surprising frequency in the past decade. The most prevalent of the eating disorders is bulimia nervosa in women who maintain a normal weight (1–4). Women with normal-weight bulimia exhibit a complex of symptoms (5) similar to that seen in patients with anorexia nervosa: disturbances of the modulation of appetite, an abnormal body image, dysphoric mood (6), and neuroendocrine abnormalities, such as menstrual dysregulation (7). In contrast to anorexia nervosa, these psychobiological disturbances cannot be attributed to weight loss, since these women maintain normal body weight.

Little is known about the pathophysiology of this disorder, but several lines of evidence raise the possibility that disturbances of one or more brain monoaminergic pathways may contribute to it. Most double-blind, placebo-controlled trials of antidepressants involving bulimic patients show that these medications reduce the frequencies of binge-eating and purging and improve mood (8). Since antidepressants are thought to exert their therapeutic effects through their actions on brain noradrenergic and serotonergic pathways, it is possible that antidepressant medications correct a disturbance of monoaminergic function in normal-weight bulimia.

The possibility of brain monoaminergic disturbances in normal-weight bulimia is further supported by considerable data on animals and humans which suggest that brain monoamine systems are important modulators of appetite, mood, and neuroendocrine function. Pharmacological studies with laboratory animals suggest that treatments which increase intrasynaptic norepinephrine or directly activate $\alpha_2$-adrenergic receptors tend to increase food consumption (9). Treatments that increase intrasynaptic serotonin or directly activate serotonin receptors tend to reduce food consumption (10, 11). Treatments that decrease dopamine activity in the lateral hypothalamus lead to hyperphagia and weight gain (12). Theoretically, greater than normal noradrenergic activity or low serotonergic or dopaminergic activity could contribute to binge-eating. Monoaminergic dysfunctions could also play a role in the dysphoric mood (13–15) and menstrual dysfunction (16, 17) commonly seen in this illness.

A limited number of data support the possibility of CNS monoaminergic disturbances in this disorder. In a preliminary study (18), a trend toward low CSF norepinephrine values was found. Brewerton et al. (19) found that normal-weight bulimic patients given *m*-chlorophenylpiperazine, a specific serotonin receptor agonist, showed less response to prolactin than control subjects, suggesting that the bulimic subjects had low serotonergic activity.

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The purpose of this study was to assess CNS monoamine neurotransmitter status in normal-weight bulimic subjects by measuring CSF levels of norepinephrine and the major metabolites of serotonin and dopamine, 5-hydroxyindoleacetic acid (5-HIAA) and homovanillic acid (HVA).

## METHOD

The subjects were 27 female patients in outpatient and inpatient bulimia nervosa treatment programs at the University of Pittsburgh (N=16) and the Medical University of South Carolina (N=11) and 14 healthy female volunteers (seven from each location). All subjects gave informed consent for the study.

The patients all met the *DSM-III-R* criteria for bulimia nervosa. All had histories of binge-eating on at least 3 or more days per week in the month before admission; 17 binged once or more per day. All purged by means of vomiting and/or laxative use. To enter the study each bulimic subject had to currently weigh more than 85% of the applicable 1959 Metropolitan Insurance Table standard for average body weight (20); the lowest weight was 88%. All but one of the patients weighed less than 122% of average body weight; the other patient weighed 133%. All but four patients had weighed more than 85% of average body weight since their early teenage years; of the exceptions, two had previously weighed between 75% and 85% and two had weighed less than 75% of the applicable average body weights.

None of the healthy volunteers had significant current or past psychiatric or medical diseases. All had normal menstrual cycles. The bulimic and healthy volunteer subjects had similar ages (mean±SD=26±6 and 29±7 years; t=1.65, df=39, p=0.11), heights (166±6 and 167±6 cm; t=0.77, df=39, p=0.45), and percentages of average body weight (103%±12% and 106%±18%; t=0.67, df=39, p=0.50). The bulimic patients had a mean±SD score on the Hamilton Rating Scale for Depression of 12±8, and the range was 0 to 30, whereas all of the healthy volunteers scored between 0 and 4. Eleven of the bulimic patients had coexisting diagnoses of major affective disorder, seven had minor affective disorders, and nine had no affective disorder diagnoses.

All 41 subjects were medication free for at least 30 days before this study. The outpatient subjects were admitted to a clinical research unit on the night before the study. The subjects fasted after midnight, were kept in bed, and were only allowed up to go to the bathroom. The lumbar punctures were performed between 8:00 a.m. and 9:00 a.m., while the subjects were in the lateral decubitus position. The CSF samples were immediately placed on wet ice and aliquoted and frozen within 1 hour. They were stored at −70 °C. The specimens used in this study were from the first 12 cc of CSF that were pooled on wet ice. Metabolite specimens were preserved in ascorbic acid. The CSF samples were assayed by means of methods previously described (21, 22). The CSF norepinephrine sample of one healthy volunteer was lost through laboratory error.

Statistical analysis was carried out with the BMDP statistical software (23). Between-group comparisons were made by means of Student two-tailed group t tests. Correlations were examined through Pearson linear regression analysis.

## RESULTS

When the samples obtained at the University of Pittsburgh were compared to those obtained at the Medical University of South Carolina, it was found that the bulimic patients and volunteers at the two institutions had similar mean values for CSF norepinephrine, 5-HIAA, and HVA (norepinephrine—t=0.12, df=25, p=0.90, and t=1.30, df=11, p=0.22, respectively; 5-HIAA—t=0.69, df=25, p=0.50, and t=1.58, df=12, p=0.14; HVA—t=0.52, df=25, p=0.61, and t=0.79, df=12, p=0.45).

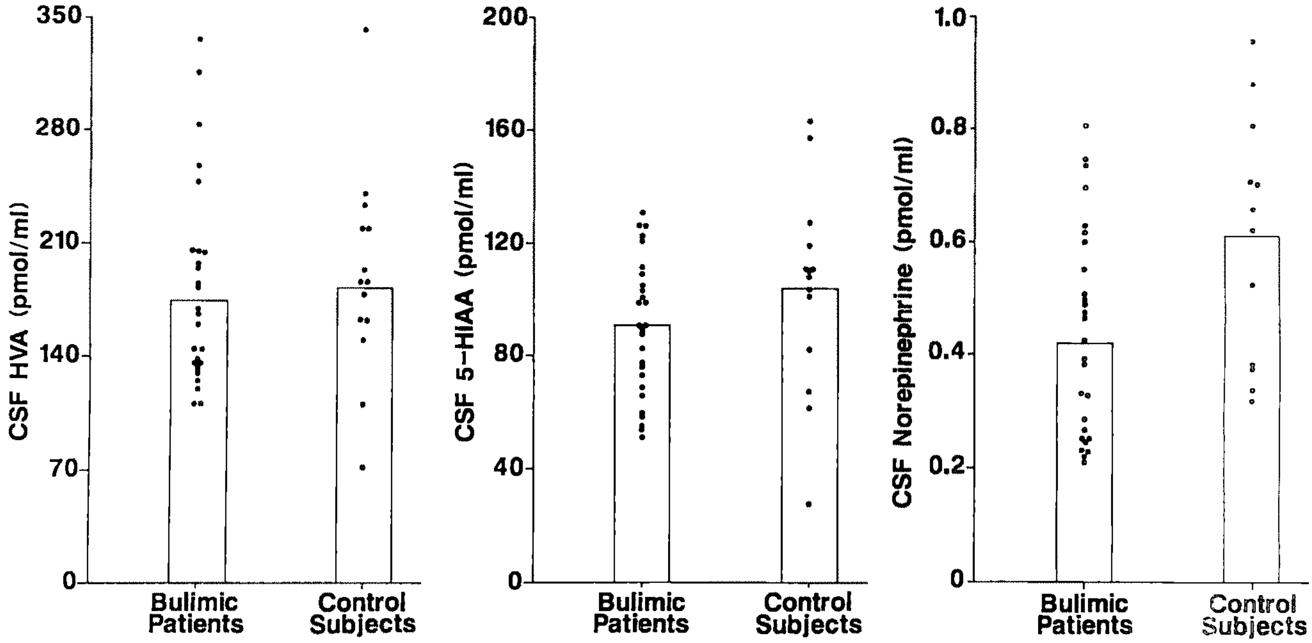
The bulimic subjects as a whole had a significantly lower mean concentration of CSF norepinephrine than did the healthy volunteer subjects (mean±SD=0.44±0.18 versus 0.58±0.21 pmol/ml; t=2.24, df=38, p=0.03). The bulimic and healthy volunteer subjects had similar concentrations of CSF 5-HIAA (91±25 versus 104±36 pmol/ml; t=1.41, df=39, p=0.17) and HVA (181±62 versus 184±64 pmol/ml; t=0.13, df=39, p=0.90) (figure 1).

Among the 27 bulimic patients only, no significant relationships were found between concentration of norepinephrine, 5-HIAA, or HVA and age (r=0.01, df=26, p=0.95; r=0.03, p=0.88; r=−0.07, p=0.74, respectively), percentage of average body weight (r=0.02, p=0.91; r=−0.03, p=0.90; r=0.26, p=0.19), or Hamilton depression score (r=−0.14, p=0.51; r=0.05, p=0.83; r=−0.04, p=0.84). The norepinephrine values of the bulimic patients with and without affective disorder diagnoses were similar; that is, the mean level of the 18 with major or minor depression was similar to that of the nine without depression (0.40±0.18 versus 0.51±0.18 pmol/ml; t=1.47, df=25, p=0.15). Similarly, the 11 patients with major depression did not significantly differ from the 16 with minor or no depression diagnoses (0.39±0.18 versus 0.48±0.19 pmol/ml; t=1.22, df=25, p=0.23).

When the bulimic subjects were subgrouped on the basis of binge frequency in the month before the study, we found that bulimic subjects who binged one or more times per day had a significantly lower mean HVA level than the bulimic patients who did not binge daily (t=2.21, df=25, p=0.04) (table 1). The values were similar for CSF 5-HIAA (t=1.38, df=25, p=0.18) and norepinephrine (t=0.59, df=25, p=0.56).

CSF 5-HIAA and HVA were significantly correlated in both the bulimic subjects (r=0.56, df=26, p<0.01) and the healthy volunteer subjects (r=0.54, df=13,

**FIGURE 1. CSF HVA, 5-HIAA, and Norepinephrine Levels of Female Normal-Weight Bulimic Patients (N=27) and Healthy Volunteers (N=14)[a]**



[a] The bars represent mean values. There was a significant difference between groups in mean norepinephrine concentration ($t=2.24$, $df=38$, $p=0.03$, two-tailed).

**TABLE 1. Relation of Binge Frequency to CSF Monoamine Concentrations in 27 Normal-Weight Bulimic Patients**

| | Six or Fewer Binges per Week (N=10) | | One or More Binges per Day (N=17) | |
|---|---|---|---|---|
| Variable | Mean | SD | Mean | SD |
| Binges per week | 3.7 | 0.9 | 17 | 13 |
| CSF 5-HIAA (pmol/ml) | 99 | 20 | 86 | 27 |
| CSF HVA (pmol/ml) | 213[a] | 50 | 163[a] | 61 |
| CSF norepinephrine (pmol/ml) | 0.47 | 0.17 | 0.42 | 0.20 |

[a] Significant difference between groups ($t=2.21$, $df=25$, $p=0.04$, two-tailed Student's t test).

$p<0.05$). Neither the bulimic patients nor control subjects showed a significant relationship between CSF 5-HIAA and norepinephrine ($r=0.14$, $df=26$, $p=0.50$, and $r=-0.07$, $df=12$, $p=0.82$, respectively) or between CSF HVA and norepinephrine ($r=0.07$, $df=26$, $p=0.72$, and $r=0.37$, $df=12$, $p=0.26$, respectively).

## DISCUSSION

This study supports the hypothesis that normal-weight bulimic subjects have a disturbance of noradrenergic function. Specifically, this study replicates and extends our previous finding (18) of a trend toward low CSF norepinephrine values in 12 normal-weight bulimic subjects. While to our knowledge there have been no other reports on CSF norepinephrine or MHPG values in bulimia, investigators at several centers have found that normal-weight bulimic subjects have lower plasma norepinephrine levels and greater β-adrenergic receptor responsiveness in the periphery than normal subjects (24, 25, and unpublished report of D.T. George et al.).

The bulimic patients in this study had a nonsignificantly lower ($p=0.17$) CSF 5-HIAA level than the healthy subjects and a similar CSF HVA level. These results are similar to findings in 37 other normal-weight bulimic patients (26). This study replicates a previous study (27) in which CSF HVA levels were lower in the bulimic patients who binged most frequently. It is not clear why low central dopamine turnover appears to be related to binge frequency or whether it is a cause or consequence of frequent binge-eating. Normal CSF 5-HIAA levels contradict the data that suggest bulimic patients are hyposerotoninergic.

It is not known whether monoaminergic abnormalities are state- or trait-related. It remains to be determined whether some defect in noradrenergic modulation of feeding behavior contributes to the pathogenesis of this illness. Alternatively, abnormalities in noradrenergic function could be secondary to a number of conditions (28–30) likely to be found in some bulimic patients, such as poor nutritional status, stress, high level of physical activity, or electrolyte disturbances. It has been theorized that a vicious circle develops in bulimia nervosa in the sense that the consequences of nutritional abnormalities perpetuate pathological behavior (31). That is, pathological eating behavior could produce starvation-related changes in noradrenergic systems (24) which foster more pathological eating behavior. Bulimia is a tenacious illness and has a high recidivism rate despite treatment (8, 32). Abnormalities in noradrenergic modulation of feeding behavior (whether primary or secondary) could contribute to such pathophysiology. This hypothesis raises the provocative question of whether antidepressant medications correct persistent monoaminergic abnormalities and thus interrupt this vicious circle.

Studies of concentrations of neurotransmitters and neuromodulators in CSF invariably raise the question of the physiological relevance of such measurements. It has been questioned whether low concentrations of CSF norepinephrine are a consequence of underactivation of the choroid plexus by the sympathetic nervous system (33) or simply reflect functional similarities in the handling of norepinephrine metabolism by the central and peripheral nervous systems (34). While the source of norepinephrine in the CSF is not known, considerable evidence (35) suggests some portion of CSF norepinephrine reflects brain and spinal cord noradrenergic neuronal activity. No methods presently available can identify the specific pathways that contribute to low CSF monoamine levels. However, it should be noted that the ability to determine CSF monoamine levels has been very useful in studies of human CNS disease. For example, low concentrations of dopamine have been found in post-mortem brain studies of Parkinson's disease (36), and such findings are reflected in vivo in lumbar CSF (37, 38). Despite the limitations inherent in CSF studies, at present there are few other techniques for directly studying these brain neuromodulators in humans in vivo.

Finally, much controversy surrounds the question of whether bulimia nervosa is a variant of affective disorders (6, 39). It is thus of interest that levels of norepinephrine in CSF and plasma have been reported to be normal or high in major depressive disorders (40–44). It has consistently been found that CSF and plasma norepinephrine concentrations tend to be low in normal-weight bulimia (18, 23, 24, unpublished study of D.T. George et al.). Moreover, antidepressants reduce the frequency of binge-eating in nondepressed bulimic patients (45, 46), and we found no relationship between depression and CSF norepinephrine levels in bulimic patients. Together these data raise the possibility that defects in noradrenergic function are independent of the presence or absence of depression in bulimia. We theorize that normal-weight bulimia is not a subtype of depressive disorder and should be considered an illness with a unique and characteristic neurobiological profile. Future studies on the effects of antidepressants in this illness should address whether these medications have specific antibulimic properties that may be related to their influence on pathways modulating appetite.

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# State-Dependent Alterations in the Perception of Life Events in Menstrual-Related Mood Disorders

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*The authors examined the reporting of daily life events by women with prospectively confirmed menstrual-related mood disorder (N=40) and asymptomatic control subjects (N=20). During the follicular and late luteal phases of the menstrual cycle, subjects completed a schedule of life events that monitors an individual's perception of 1) the frequency of occurrence of life events and 2) the degree of associated distress or pleasure. The patient group reported significantly more negative life events than the control group. Further, the patients with menstrual-related mood disorder showed significantly more distress associated with the same event when it occurred in the premenstrual phase than when it occurred in the postmenstrual phase.*

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Menstrual-related mood disorders consist of a heterogeneous group of affective and somatic symptoms that occur in a phase-specific manner during the late luteal phase of the menstrual cycle. The occurrence of stressful life events has been reported to influence the onset and course of both psychiatric and medical illnesses, including menstrual-related mood disorders (1, 2). Nevertheless, the exact nature of the relationship between life events and psychiatric or medical illness remains poorly understood. Birley and Connolly (3) have proposed several possible interactions to describe the reported relationship between life events and the onset of illness. Thus, the reporting of stressful life events 1) may be as much a reflection of the patient's emotional state when ill as it is a factor related to onset of illness, 2) may be based on the patient's expectations and beliefs regarding connections between stress and the onset of illness, 3) may be related to the disruptive effects of either the prodrome of the illness or the illness itself on an individual's environment, and 4) may reflect characterological traits in the patients studied that lead to the overreporting of *both* symptoms and life events.

As part of our interest in the state model of psychological functioning, we were interested in whether patients with prospectively confirmed menstrual-related mood disorders would exhibit state-dependent changes in perceptions of daily life events that occurred in a manner specifically related to menstrual cycle phase. In order to more clearly delineate the extent to which life events interact with menstrual-related mood disorders, we longitudinally investigated the pattern of reporting of life events in women with menstrual-related mood disorders and in asymptomatic volunteers (control subjects) during both follicular (nonsymptomatic) and late luteal (symptomatic) phases of the menstrual cycle.

## METHOD

### *Subjects*

The subjects for this study were 40 women with prospectively confirmed menstrual-related mood disorders (ages 29–45 years) and 20 asymptomatic female volunteers (ages 22–45 years). All of the patients and volunteers were self-referred to our clinic in response to advertisements in the local newspapers and hospital newsletter. All subjects reported regular menstrual cycle lengths, ranging between subjects from 21 to 30 days. Neither patients nor volunteers were taking psychoactive medications, hormonal preparations (including oral contraceptives), mineral supplements, or nonsteroidal anti-inflammatory medication. Patients were free of current (both at intake and time of testing) and recent (within the past year) medical illness and were also free of current and recent (within the past 2 years) psychiatric illness, determined by administration of the Schedule for Affective Disorders and Schizophrenia—Lifetime Version (SADS-L) (4). Axis II psychiatric diagnoses were not determined in our patient sample. Volunteers were also free of current and past psychiatric illness, as determined by a modified SADS-L interview, and were free of current medical illness.

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Before their entry into the study, all patients had the timing and severity of their mood symptoms prospectively confirmed by daily visual analogue scale self-ratings, as described previously (5). All patients participating in this study had mean negative mood (depression, anxiety, irritability) symptom self-ratings that increased by 30% (of the used range of the scale) in the week before menses compared with the week after menses for at least two of three cycles after the initial screening interview. These criteria are a slightly more stringent version of the criteria adopted by the National Institute of Mental Health Premenstrual Syndrome Research Workshop Workgroup in 1983; the only difference is the specification of a 7- rather than a 5-day interval before and after menses. Approximately 30% of the patients presenting to our clinic with complaints of premenstrual syndrome meet these diagnostic criteria. We retrospectively examined records of patients participating in this study and found that each of the 40 patients selected for participation met *DSM-III-R* criteria for late luteal phase dysphoric disorder.

Control subjects were women who reported no change in mood and behavior in relation to menstrual cycle phase and who also showed no evidence of menstrually related mood changes when studied for two menstrual cycles with the same self-rating scales as those used in the patient group. Volunteers received monetary reimbursement for their participation in this study.

### *Procedure*

Each subject completed a modification of Lewinsohn's Pleasant and Unpleasant Events Schedule (6, 7) during both the follicular (nonsymptomatic) and the late luteal (symptomatic) phases of the menstrual cycle. The modified schedule employed is a 111-item self-report scale that monitors an individual's perception of 1) the frequency of occurrence of life events and 2) the degree of pleasantness associated with each life event, during the 5 days before scale completion. Events were categorized as positive, negative, or neutral life events on the basis of the patient's rating, on a 7-point scale (from −3 to +3), of that particular event during either the late luteal or follicular phase of the menstrual cycle. For example, a patient who assigned a rating between −1 and −3 to a particular event would have that event categorized as negative, whereas a rating of +1 to +3 would result in that event being rated as positive. An event rating of 0 defined a neutral event.

All subjects were concurrently administered the Beck Depression Inventory and the Spielberger State Trait Anxiety Inventory—State Form during each phase of testing to confirm the presence of significant mood change between the first and second completions of the events schedule. We were unable to obtain paired depression and anxiety scores for 10 patients and three control subjects.

In the midst of this study and after preliminary data analysis, we decided to assess the stability of our initial findings over time. To this end, samples of 15 patients and 15 volunteers were retested during a subsequent menstrual cycle (2–3 months after the original testing). On the basis of our preliminary findings a power analysis was performed to calculate the minimum sample size needed in this study, with a power of 80% and a type I error (alpha) of 0.05. We determined that sample sizes of at least 12 subjects in each retest group would be necessary to detect significant changes in the reported occurrence of negative life events and to avoid a type II statistical error.

### *Analysis*

The relationship between menstrual cycle phase and the reported frequency of occurrence of positive, negative, and neutral life events in patients and control subjects were analyzed by analysis of variance (ANOVA) with repeated measures, with menstrual cycle phase and diagnostic groups (patients and control subjects) as the independent variables. We employed the Bonferroni inequality method to adjust the p values in the analysis of individual group mean differences in order to make a post hoc correction of the probability of making a type I statistical error. This procedure was indicated because of the number of post hoc t tests performed in our analysis and the associated risk of making type I statistical errors. Menstrual cycle phase-related changes in the degree of perceived pleasantness of events schedule items were analyzed by Student's t test in patients and control subjects.

The relationship between menstrual cycle phase and depression and anxiety scores in patients and control subjects were analyzed by ANOVA with repeated measures, with menstrual cycle phase and diagnostic group as the independent variables. Individual group mean differences were analyzed by Bonferroni t tests. Finally, the relationships between menstrual cycle phase-related changes in depression and anxiety scores and menstrual cycle phase-related changes in the perceived pleasantness of events schedule items were examined with Spearman correlation coefficients.

## RESULTS

The total number of events schedule items endorsed as occurring during the follicular and late luteal phases did not differ between patients and control subjects ($F=1.18$, $df=1, 58$, $p>0.05$). The events that occurred included both events that were rated as identical in pleasantness during both menstrual cycle phases and those which were rated as different in degree of pleasantness in the late luteal phase and the follicular phase. The number of items rated as identical in degree of pleasantness (no change) in the follicular and late luteal phases was not significantly different between the patient and control groups. However, patients reported significantly more events schedule items as changing in degree of pleasantness from the follicular

**FIGURE 1. Change in Degree of Pleasantness for Events Schedule Items From the Follicular Phase to the Late Luteal Phase for 40 Women With Menstrual-Related Mood Disorders and 20 Normal Female Control Subjects**

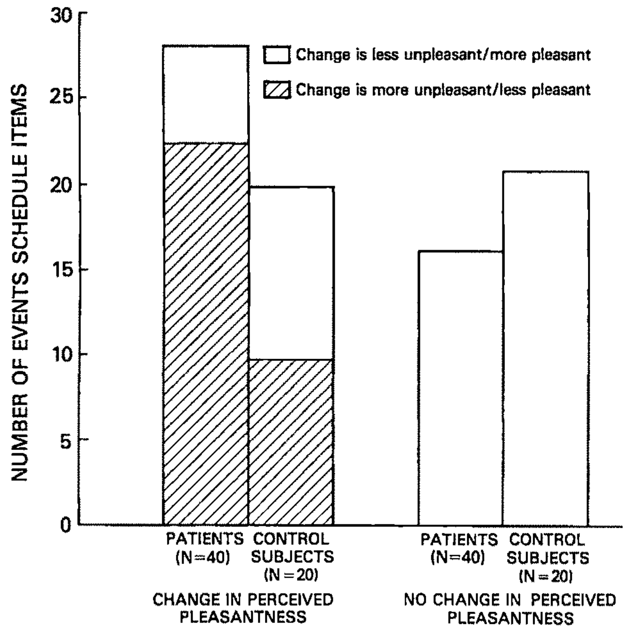

**TABLE 1. Number of Events Schedule Items Rated as Negative in the Follicular and Late Luteal Phases by 40 Women With Menstrual-Related Mood Disorders and 20 Normal Female Control Subjects**

| | | Number of Events Rated as Negative | | | |
|---|---|---|---|---|---|
| | | Follicular Phase | | Late Luteal Phase | |
| Group | N | Mean | SD | Mean | SD |
| Patients with menstrual-related mood disorders | | | | | |
| Test | 40 | 22.08 | 15.13 | 42.73[a] | 22.70 |
| Retest | 15 | 19.07 | 15.54 | 34.87[a] | 14.07 |
| Control subjects | | | | | |
| Test | 20 | 10.65 | 5.55 | 13.15 | 9.09 |
| Retest | 15 | 14.00 | 11.86 | 12.53 | 11.19 |

[a] Patients reported significantly more negative life events in the late luteal phase (Bonferroni t=6.67, df=58, p<0.01), but not the follicular phase (Bonferroni t=2.4, df=58, p>0.05), than did control subjects. Patients also reported significantly more negative life events during the late luteal phase than in the follicular phase (Bonferroni t=7.75, df=58, p<0.01).

to the late luteal phase than did the control group (t=3.85, df=58, p<0.001, two-tailed test) (figure 1). Patients reported significantly more events schedule items as becoming less pleasant or more unpleasant during the late luteal phase compared with the follicular phase than did control subjects (t=5.09, df=58, p<0.001). In addition, the patients reported significantly fewer events schedule items as becoming more pleasant during the late luteal phase compared with the follicular phase than did control subjects (t=2.22, df=58, p<0.05).

The occurrence of a substantial change in perceived pleasantness of an event in the late luteal phase, compared with the follicular phase, was evaluated by examining items that changed by at least 2 scale points. Patients reported significantly more events schedule items as substantially more unpleasant during the late luteal phase than in the follicular phase, compared with the control group (t=4.86, df=58, p<0.001). Events schedule items that showed substantial changes included the following: pressure at work, having a frank and open conversation, being told I am needed, and reading the newspaper. However, there was a large individual variation among patients with respect to those schedule items which showed substantial change across the menstrual cycle. There was no significant difference between patients and control subjects in the number of events schedule items that were rated as substantially less unpleasant or more pleasant during the late luteal phase, compared with the follicular phase.

Menstrual cycle phase-related changes in the perception of occurrence of negative life events during the test and retest conditions were also observed (table 1). ANOVA with repeated measures of the test data showed a significant Time by Diagnosis effect (F=15.51, df=1, 58, p=0.0002), as well as significant effects for diagnosis (F=29.31, df=1, 58, p<0.0001) and time (F=25.22, df=1, 58, p<0.0001). Patients reported significantly more negative life events occurring in the late luteal phase, but not in the follicular phase, than did control subjects. Patients also reported the occurrence of significantly more negative life events during the late luteal phase than in the follicular phase. This phase-related change in the perception of occurrence of negative life events was not demonstrated in the control group (Bonferroni t=0.66, df=58, p>0.05). Retesting samples of 15 patients and 15 control subjects 2 to 3 months after the initial testing showed a similar significant late luteal phase increase in the occurrence of negative life events in the patient sample (ANOVA with repeated measures, Time by Diagnosis: F=14.45, df=1, 28, p=0.001; Bonferroni t=4.9, df=28, p<0.01).

Similarly, menstrual cycle phase-related changes in the perception of the occurrence of positive life events were observed in patients but not in control subjects. ANOVA with repeated measures of the test data showed a significant Time by Diagnosis effect (F=7.78, df=1, 58, p=0.007), as well as a significant effect of time (F=21.16, df=1, 58, p<0.001). Patients reported the occurrence of significantly fewer positive life events during the late luteal phase than did control subjects (Bonferroni t=3.2, df=58, p<0.01). Patients also reported the occurrence of significantly fewer positive life events during the late luteal phase than in the follicular phase of the menstrual cycle (Bonferroni t=6.55, df=58, p<0.01). Similar Time by Diagnosis effects were demonstrated during the retest conditions

(F=8.76, df=1, 28, p=0.006), and patients reported the occurrence of significantly fewer positive life events during the late luteal phase than in the follicular phase (Bonferroni t=3.28, df=28, p<0.01).

Patients showed no difference from control subjects in their follicular (nonsymptomatic) phase scores on the Beck Depression Inventory (Bonferroni t=0.96, df=45, p>0.05) and the Spielberger State Trait Anxiety Inventory (Bonferroni t=0.4, df=45, p>0.05). However, significant differences were found in the patients' scores between the late luteal (symptomatic) phase of the menstrual cycle and the follicular phase on the Beck Depression Inventory (Bonferroni t=7.8, df=45, p<0.01) and the Spielberger State Trait Anxiety Inventory (Bonferroni t=5.14, df=45, p<0.01). Further, patients had significantly higher depression scores (Bonferroni t=7.08, df=45, p<0.01) and anxiety scores (Bonferroni t=6.14, df=45, p<0.01) than the control group during the late luteal phase of the menstrual cycle. There was no correlation between the magnitude of change in the depression and anxiety scores and the change in perception of either the number of items becoming more unpleasant or the reported change in the occurrence of negative life events during the late luteal phase of the menstrual cycle.

## CONCLUSIONS

Patients reported 1) a significant increase, compared with control subjects, in the number of life events rated as more unpleasant/less pleasant during the late luteal phase versus the follicular phase of the menstrual cycle; and 2) a significant increase, compared with control subjects, in the occurrence of perceived negative life events and a significant decrease in the occurrence of perceived positive life events during the late luteal phase versus the follicular phase of the menstrual cycle. Thus, the same events were rated by the patients as becoming more unpleasant and the occurrence of unpleasant events was more frequent during the late luteal phase of the menstrual cycle.

The differences we observed between patients and control subjects in the perception of both the occurrence and degree of unpleasantness of negative life events were largely confined to the late luteal phase of the menstrual cycle. Further, patient differences were not due to patients endorsing a larger proportion of the events schedule items than control subjects during either phase; this suggests that the perception of change in both frequency and degree of pleasantness of life events is not related solely to the presence of a chronic illness (menstrual-related mood disorders), nor is it related solely to characterological traits that result in the overreporting of both symptoms and negative life events. Our data do suggest that the observed changes in the perception of life events are either representative of state-dependent alterations in both mood and perception or the result of the interaction between the patient's affective state during the late luteal phase and her environment.

State-related alterations in affect, perception, and behavior are important in the phenomenology of menstrual-related mood disorders. Wolff (8) has emphasized that a state represents a discrete, self-organizing pattern of experiential variables; while each of the discriminating variables is continuous and may exist along a dimension of severity, it is the pattern or clustering of variables rather than the intensity of any single variable that determines the state. The application of the state model to menstrual-related mood disorders would suggest the following: First, menstrual-related mood disorders may be seen not as a symptom-specific disturbance but rather as a disorder defined by a menstrual cycle-linked transition into a particular experiential state that is usually (although not exclusively) characterized by dysphoria or irritability. This concept is suggested by the work of Stewart et al. (9), who suggested the role of state-dependent phenomena in premenstrual syndrome following their observations of state-dependent learning in animals receiving progesterone. In addition, Hammond and Keye (10) have reported significant changes from the follicular to the late luteal phase in nine of 12 scale scores of the MMPI, an instrument that is supposedly a trait measure. Second, the state model would predict that the severity of individual symptoms of menstrual-related mood disorders may vary independently, contrary to what would be expected if one symptom were epiphenomenal to another. In our sample of women with menstrual-related mood disorders, late luteal phase affective changes were recorded by both the Beck Depression Inventory and the Spielberger State Trait Anxiety Inventory. However, there was no correlation between either the late luteal "symptomatic" phase scores or the change in these instruments' scores across the menstrual cycle and the observed changes in either the number of reported negative life events or the degree of change in perceived pleasantness of life events during the late luteal phase. Thus, the severity of affective change in the patients, as measured by the Beck and Spielberger inventories, did not correlate with the severity of perceptual change, which might be expected if the premenstrual mood state represented an exaggerated form of molimina (11).

In conclusion, our findings suggest that many women with prospectively confirmed menstrual-related mood disorders experience both marked changes in affective valence and state-related changes in perception of daily life events during the late luteal phase of the menstrual cycle. Thus, symptoms of menstrual-related mood disorders may best be conceptualized as occurring in an experiential state that is characterized by both affective and cognitive components. Such a model would appear consonant with clinical reports of profound menstrual cycle-related differences in a patient's experience of both self and environment. While the role of life events in the experience of symptoms of menstrual-related mood disorders is unclear, the ability of life events to modulate symptoms is frequently reported. Our data suggest that reported changes in the impact of life events may as much reflect the state-related change in perception of life events as they do a direct effect of altered or stressful life circumstances.

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# Three Cases of Anorexia Nervosa Associated With Temporal Lobe Epilepsy

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*The authors present case reports of three patients with temporal lobe epilepsy who developed anorexia nervosa. All three patients showed both affective disorder and dysmorphic delusions, which were probable contributors to the appearance of the eating disorder.*
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Despite the relative frequency of both anorexia nervosa and temporal lobe epilepsy, few reports of an association between the two have been published, and a standard text (1) does not suggest any correlation. Organic factors in anorexia nervosa are underreported; EEG abnormalities have been reported in only a few patients, usually compulsive eaters (2, 3). We report three cases of anorexia nervosa associated with temporal lobe epilepsy.

## CASE REPORTS

*Case 1.* Ms. A, a right-handed woman of normal development, 5 ft 5½ inches tall, had suffered head trauma, with brief loss of consciousness and projectile vomiting, at age 6. At 13 years of age she began to have generalized tonic-clonic seizures; these recurred only yearly, although she had several episodes of status epilepticus. When she was 25 years old, a fall caused intracerebral bleeding that required a partial right frontotemporal lobectomy. Following surgery Ms. A was hospitalized for 7 months for an episode of agitation, overactivity, extroverted behavior, thought disorder, and refusal to eat; she had lost 77 lb. She responded partially to neuroleptics. Subsequently, she developed "staring" episodes without automatisms (partial complex seizures).

At age 36 Ms. A was admitted to the hospital because of outbursts of aggressive behavior and an eating disorder. She was restricting her intake of food and fluids, denying hunger, and secretly vomiting. She had become a vegetarian, and she believed that she was grossly overweight despite her thin appearance. She justified not eating on the basis of examples of Biblical figures, starvation in the world, and God's command. Her weight had remained stable at about 100 lb. There was no family history of neuropsychiatric disorders or substance abuse.

Ms. A had frequent 3- to 9-second staring spells, but she easily returned to contact with the environment. There was no psychomotor retardation or agitation. Her affect was flattened, and hyposexuality, hyperreligiousness, and philosophical concerns were noted. Her digit span was five digits forward and three in reverse. Her ability to do confrontation naming and word list generation tasks was mildly deficient, but results on tests of short-term verbal and nonverbal memory were normal. She could accomplish only simple rote calculations; concreteness and perseveration of thought were present. Muscle tone and reflexes were mildly increased on the left. Right superior quadrant sensory extinction was present on double simultaneous stimulation, and right "mirror" movements and bilateral asterixis were observed.

Ms. A had had only two menstrual periods in the 10 years following the lobectomy, but there was no galactorrhea, hirsutism, or thyromegaly. A Pap smear showed atrophic cervical cells. Her prolactin level was 48 ng/ml, her morning cortisol level was low normal, her follicle-stimulating hormone level was 5 IU/ml, and her luteinizing hormone level was 3 IU/ml. Her free $T_4$ index was in the low normal range. She had mild leukopenia with megaloblastic changes due to malnutrition. Her medications included valproic acid, carbamazepine, benztropine, fluphenazine, and conjugated estrogens. Her EEG showed a generalized spike and wave pattern superimposed on a slow background frequency, with right frontal and midtemporal foci. A CT scan showed brain tissue loss in the right posterior frontal regions and compensatory expansion of the right lateral ventricle.

*Case 2.* Ms. B, a 25-year-old right-handed woman of average intelligence, 5 ft 7 inches tall, started having seizures at age 13. These consisted of a brief interruption of consciousness followed by facial movements and standing up. One generalized seizure occurred when she was 23 years old. Past treatment included phenytoin plus carbamazepine and carbamazepine plus valproic acid.

Ms. B reported frequent episodes of transient depression, at least one episode of major depression, and several attempts at suicide. She also had occasional ideas of reference and auditory hallucinations (not directed at her), but hyperreligiousness and hypergraphia were not present. The patient's eating disorder had begun at age 17; she had exercised excessively, vomited, and taken diet pills, laxatives, and diuretics, but she had never binged. She had considered committing suicide if she gained weight. Her maximum weight had been 168 lb, but she had reduced her food intake to the point of complete starvation to bring her weight into the

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mid-120s. Despite appearing emaciated she insisted that the lower half of her body was still fat.

The patient's father is an alcoholic, and her mother and two siblings are epileptic. The mother has also been treated with antidepressants and thyroid supplements for depression. One sister and two brothers have psychiatric disorders of an unknown nature.

On examination Ms. B was an emaciated, intense young woman whose affect was only mildly restricted. Her attention, language, memory, constructions, calculations, and performance on frontal systems tasks were all within normal limits, and results of a neurologic examination were normal. Her EEG showed intermittent sharp 5- to 7-cycles/sec slow waves and irregular 3- to 4-cycles/sec slow waves in the left frontotemporal region; a CT scan of the brain was normal.

*Case 3.* Ms. C, a 28-year-old ambidextrous woman with a high school education, 5 ft 10 inches tall, reported frequent episodes of depression with suicidal ideation, including six suicide attempts. Her mood was labile, with almost continuous ruminations over how she should feel or react. She was hypergraphic, maintaining copious diaries over many years. Libido was absent. There was no nascent philosophical or religious concerns, but she was unable to distinguish important from trivial events. It was uncertain which neurovegetative symptoms had appeared during past episodes, but neither these nor signs of mania were present on examination; many of these episodes had been associated with amnesia.

Ms. C reported that she had had bulimic episodes since she was 11 years old, most of which were followed by vomiting. The binges have decreased in intensity and frequency but still occur approximately once every 2 weeks. Her current (and highest) weight is 183 lb, with an average of 155 lb (5–10 lb above ideal), and her lowest weight was 128 lb. Some years earlier she had lost a quarter of her weight, believing that she was grossly overweight, particularly below her waist; she was obsessed with dieting and thinness, stopped menstruating, and abused diuretics, ipecac, and laxatives. Treatment with neuroleptics, tricyclic antidepressants, and benzodiazepines was unsuccessful. Tricyclic antidepressants produced periods of confusion and exacerbated her state. There was no family history of neurologic or psychiatric illness.

Ms. C's thought form was tangential and viscous. Although her cognitive functions were normal, results of tests of executive functioning, including the alternating hand, Luria three-hand, and reciprocal finger sequences tests, were abnormal. Results of a neurologic examination were normal except for mild bilateral dystonic posturing of her hands while she was walking. An EEG showed diffuse paroxysmal activity. Carbamazepine produced some improvement, and the addition of lithium to the anticonvulsant regimen normalized both her affective state and the eating disorder.

## DISCUSSION

All three patients reported classic anorexia nervosa (*DSM-III-R*), with refusal to maintain body weight, an intense fear of gaining weight, a disturbance in the way in which their body weight, size, and/or shape was experienced, and amenorrhea. Two of the patients showed overt seizure disorder, and the third, who also had bulimia nervosa, had amnestic periods with prolonged psychotic mood change and hypergraphia, viscosity, and hyposexuality as probable epileptic manifestations. In each patient the eating disorder began after the appearance of ictal symptomatology. Depression was a major factor in all three cases; the patient in case 2 had a family history of mood disorder and epilepsy.

The association between epilepsy and eating disorders probably relies on several mechanisms, including neural control over body image and appetite, mood disorders, and psychosis. The body image disturbance of anorexia nervosa straddles the boundary between somatoform disorders (dysmorphophobia, or body dysmorphic disorder [4]) and delusional disorders, somatic subtype (*DSM-III-R*). While the term "dysmorphophobia" refers to a preoccupation with an imagined defect in appearance, implying a mild or neurotic disturbance, many patients with this disorder are severely ill. Schachter (5) showed that this single term spanned a variety of cases, with two patients having a "dysmorphic delusion," as opposed to a neurotic worry, about ugliness. Two patients whose cases were presented by Andreasen and Bardach (6) had diagnoses of personality disorders with schizoid and compulsive features—as did 11 of the patients in Hay's series (7)—although both of these patients had family histories of severe mood disorder.

The term "body schema" is used primarily for the awareness of the spatial characteristics of one's body, formed by ongoing and past sensory information, while "body experience" encompasses psychological and situational factors as well (8). Distortions of body schema involve a unilateral misperception ranging from complete lack of awareness of paralysis (anosognosia) to indifference (anosodiaphoria) and hostile personification (misoplegia) (9), although these tend to fade over time. Neglect syndromes often occur, with hemi-inattention and hemispatial neglect as the more stable features. These syndromes are apparent in injury not only to the parietal (association) cortex but to the prefrontal cortex and in thalamic lesions; the most common area involved is the posterior temporoparietal cortex in the watershed between the middle and posterior cerebral artery territories. Microsomatognosia and macrosomatognosia—the perceptions that bodily parts are abnormally small or large, respectively—also occur most often in the setting of a paroxysmal disorder (8) and may affect the content of delusions.

Bilateral asomatognosias result more frequently from dominant hemisphere lesions, especially in the posterior parietal lobe. The temporal lobes receive visual, auditory, proprioceptive, and other relevant sensory information from the secondary sensory areas; in turn this information provides input to the limbic system through the entorhinal area, integrating it with interoceptive data from subcortical and diencephalic structures (9).

A study of the etiologies of weight loss and the localization of brain tumors associated with weight loss showed that right hemisphere tumors were present twice as often as those on the left, and nearly all were in the anterior regions (10). In two patients this was due to a bizarre diet or compulsive food rituals; one man with a frontal lobe grade II astrocytoma had lost 35 lb but refused to consider a diet other than the macrobiotic one he used, and a diabetic woman with a left temporal lobe grade IV astrocytoma had lost 45 lb because of her refusal to eat meat and compulsive adherence to her diabetic diet (J.L. Griffith, personal communication, 1989). Lesions of the amygdala often disrupt appetite by disturbing facilatory and inhibitory control over hypothalamic systems. Bilateral lesions of the orbitofrontal prefrontal cortex in animals lead to the lateral hypothalamic syndrome with aphagia.

Although most of the hormonal and hypothalamic changes in anorexia nervosa have been attributed to the loss of body weight and negative caloric balance, primary lesions in the hypothalamic region can produce a syndrome that resembles anorexia nervosa. The diencephalic syndrome of early childhood presents with severe emaciation despite a normal appetite, normal alertness, and mood and locomotor overactivity; a tumor in the hypothalamic and third ventricular area, invading or exerting pressure on the anterior regions, has been thought to be responsible. Similar behaviors have been produced in animals with lesions of the frontohypothalamic tracts and medial hypothalamic nuclei. Cyclic vomiting attributed to simple partial seizures due to a medial posterior temporal lobe focus has been reported (11). In adults, hypothalamic tumors have been reported to cause syndromes mimicking anorexia, and emaciation alone may appear in up to 18% of patients with hypothalamic lesions (12).

Mood disorders are common with seizure disorders (13) and are also associated with anorexia nervosa; rates of affective symptoms range from 5% to 85%, and the suicide rate is approximately 4%, with an increase over time (14). Half of 17 prospective studies demonstrated a subsequent episode of depression in more than 15% (15%–45%) of their anorexic subjects (15). There is evidence for considering anorexia nervosa to be a variant of mood disorder in certain patients on the basis of clinical features, longitudinal course of illness, family history, similarities in the abnormalities of adrenocortical and thyroid activity and catecholamine metabolism, and pharmacologic response to antidepressants (15). However, this association is not clear and has been contested by various authors because of the complicated relationships among mood disorders and their interaction with physical illness (16).

The type of eating disorder associated with psychosis is controversial. In a group of 84 schizophrenic patients (17), abnormalities in eating behavior were widespread; two-fifths had delusional eating disorders, one-sixth had perceptually based eating disorders, half had deviant eating behavior, two-fifths had dysfunction associated with psychotropic medication, and one-quarter had neurotic symptoms with respect to food intake. However, only one schizophrenic woman fulfilled the *DSM-III* criteria for anorexia nervosa. A report by Hsu et al. (18) identified six patients with schizophrenia in a series of 105 with anorexia nervosa. However, five of these had depression that preceded the schizophrenia-like psychosis, and one later developed hypomania. One had had teeth extracted because of a "dysmorphic" delusion. Thus, the eating disorder seems to have been more closely associated with affective than with schizophrenic psychosis.

Psychosis can occur with seizure disorder, particularly when there is a dominant temporal lobe focus (19). It has been suggested that this localization reflects an injury to the integrated limbic-subcortical system that mediates mood, motivation, and motion (20). Limbic ictus, in particular the kindling phenomenon in the amygdala, has been postulated to be responsible for the symptoms of atypical psychoses. A prolonged discharge can lead to dramatic changes in behavior that may persist for months before remitting and that resemble almost any form of psychopathology, particularly atypical affective and schizophrenic disorders (21).

In the three patients with temporal lobe epilepsy that we have described, several mechanisms for the onset of anorexia nervosa are possible. The eating disorder appeared to be associated with an affective psychosis generated and conditioned by the seizures. The main delusion was a dysmorphic or somatic one concerning body image. This delusion was the necessary condition for the appearance of the other features of the anorexic syndrome. We suggest that a functional disturbance in the limbic regions may produce or exacerbate the full syndrome of anorexia nervosa.

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# Treatment of Alzheimer's Disease With Short- and Long-Term Oral THA and Lecithin: A Double-Blind Study

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*Ten Alzheimer's disease patients underwent a trial of oral tetrahydroaminoacridine (THA) and lecithin. After 3 inpatient weeks there was no clear therapeutic effect. Three of six patients able to continue in long-term treatment showed measurable cognitive improvement, but only one displayed clinically obvious improvement.*

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Effective palliative treatment for Alzheimer's disease has been an elusive goal for clinicians and researchers. Attempts to enhance central synaptic acetylcholine by the use of anticholinesterases such as physostigmine and tetrahydroaminoacridine (THA, or tacrine) have been particularly interesting. THA has produced improved learning and memory in rodents (1, 2) and nonhuman primates (3, 4) and has shown the most promise in improving cognition in Alzheimer's disease (5, 6). We report here our experience with oral THA in 10 patients with Alzheimer's disease.

## METHOD

### Inpatient Phase

Ten male patients 62 years of age or older met the criteria for probable Alzheimer's disease of the National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer's Disease and Related Disorders Association (7) and were admitted to our geropsychiatry unit. Their mean±SD age was 70.3±4.9 years, and their mean±SD number of years of schooling was 13.6±4.0. Informed consent was obtained from the patients or their conservators, psychotropics were withdrawn, and the patients were behaviorally stabilized over at least a 2-week period. All of the subjects received baseline neuropsychological and laboratory evaluations.

In the THA dose-finding phase of the study, the subjects received commercial lecithin (55% phosphatidylcholine), 30 g/day p.o., for at least 2 weeks before the administration of THA and throughout the inpatient phase. Serum choline concentrations were monitored before and 2 weeks after the lecithin was started. After the 24-hour time course of the serum THA concentration for a single oral dose had been determined, THA (1,2,3,4,tetrahydro-9-aminoacridine hydrochloride; Aldrich Chemical Co., Milwaukee, Wis.) was given in oral doses increased by 25 mg/day to a maximum of 250 mg/day or until cholinergic side effects were noted. A daily assessment of vital signs, ECG, serum THA concentration, Mini-Mental State examination score, and Controlled Oral Word Generation Test score was made 2 hours after THA ingestion. The dose that did not produce side effects but resulted in the highest Mini-Mental State and word generation scores was selected as the best daily dose for each subject.

After a 48-hour THA-free period, the subjects were randomly assigned to their best doses of THA plus

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lecithin or to placebo and lecithin during week 1. During week 2 they were THA free (placebo and lecithin only), and during week 3 they received the treatment that had not been given during week 1. Serum THA levels were determined after this double-blind phase by a modification of the high-performance liquid chromatographic method of Park et al. (8).

The patients' vital signs and ECGs were checked daily. Weekly monitoring consisted of routine laboratory tests and side-effect and medication checklists. The Mini-Mental State examination and the oral word generation test were given at baseline and twice weekly. Weekly tests consisted of the Fuld Object Memory, the Digit Span, and the Trail-Making tests, an immediate and delayed paragraph recall test, a name-learning test, and an orientation test. Serum THA levels were determined at the time of testing. Baseline and weekly double-blind behavioral measures included the Activities of Daily Living and Instrumental Activities of Daily Living scales, the Nurses' Observation Scale for Inpatient Evaluation, the Global Deterioration Scale (9) (for determining stage of dementia), and weekly written observations by spouses.

### *Outpatient Phase*

Six of the 10 inpatients continued in the study as outpatients. Three patients did not enter the outpatient phase because of substantial elevation of their hepatic enzyme levels, and a fourth was institutionalized because of the progression of his Alzheimer's disease. Four months elapsed between the inpatient and outpatient phases.

New baseline measures were taken for the outpatient phase. These included routine laboratory tests and a set of measures consisting of the Mini-Mental State, the Controlled Oral Word Generation Test, the Global Deterioration Scale, the Alzheimer's Disease Assessment Scale (10), and the Geriatric Evaluations by Relatives Rating Instrument.

After the baseline measures had been taken, but before the patients entered the randomized, double-blind phase, all patients received lecithin (>75% phosphatidylcholine; PhosChol, Elizabeth, N.J.), 9 g/day, for 2 weeks. The outcome measures were repeated at the end of these 2 weeks. Thereafter, lecithin was continuously given throughout the double-blind phase. All patients received their best THA doses, as determined in the inpatient phase of the study. However, because of the previous liver enzyme abnormalities, the maximum dose was reduced from 250 to 200 mg/day. One subject (patient 1), who experienced mild enzyme elevation at a dose of 125 mg/day, was given 75 mg/day. Subjects then entered the double-blind, randomized, crossover part of the study, which consisted of five consecutive 2-week periods: one 2-week period of placebo and lecithin and four 2-week periods of THA and lecithin. Outcomes were evaluated at the end of each 2-week period. After completion of the double-blind phase, a 2-week, placebo-only period was observed and evaluated.

### *Statistical Analysis*

An overall analysis of variance (ANOVA) with repeated measures on one factor was used for the inpatient phase. Additionally, to investigate the possibility of individual responders to THA, results of each of 11 cognitive and behavioral tests administered to each patient were scored as positive or negative. The proportion of positive responses for each person at baseline was compared to the same proportion when that person was taking THA and lecithin. Both chi-squares and exact p values under the binomial distribution were computed to judge the significance of improvement in each patient. The average overall proportion of positive responses at baseline for all 10 patients was also compared to the average proportion of positive responses during the drug conditions, and the difference was assessed with a chi-square test. The outpatient group's Mini-Mental State score change under the drug conditions was assessed by the Wilcoxon signed-ranks test. For individual patients, change under the drug conditions was evaluated by the Wilcoxon rank-sum test.

## RESULTS

### *Inpatient Phase*

All subjects completed the 24-hour time-course study. The mean±SD peak serum level of THA was 6.25±3.21 ng/ml; this was achieved 2–3 hours after a 50-mg oral dose. The THA concentration returned virtually to zero in 24 hours.

Best doses ranged from 100 to 250 mg/day. Two patients' test scores did not identify a specific best THA dose. For them, the highest tolerated dose was designated as the best dose. Six of the 10 subjects experienced peripheral side effects with doses above 125 mg/day and with serum concentrations ranging from 12 to 44 ng/ml. The side effects included sinus bradycardia and tachycardia, nausea, vomiting, and diaphoresis. The side effects were not strictly proportional to doses or serum THA concentrations and disappeared with dosage reduction. Results of laboratory tests were normal during the dose-finding phase.

Not all subjects were able to complete the entire weekly neuropsychological battery. However, scores for all 10 subjects were obtained on the Mini-Mental State, the oral word generation and orientation tests, and the Global Deterioration Scale.

An overall ANOVA with repeated measures for test scores on trials revealed no significant difference between the drug and nondrug conditions for all neuropsychological test scores and no effects of order of presentation of the drug. The mean±SD serum THA

TABLE 1. Mini-Mental State Examination Scores of Six Alzheimer's Disease Patients During Periods With and Without Treatment With THA

| | | | Mini-Mental State Score | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | | Periods Without THA[a] | | Periods With THA[b] | | | |
| Patient | Age (years) | Education (years) | Mean | SD | Mean | SD | Change[c] | % Change[d] |
| 1 | 65 | 12 | 23.25 | 1.50 | 23.00 | 0.82 | −0.25 | −0.8 |
| 3 | 74 | 20 | 11.00 | 0.82 | 18.25 | 1.89 | +7.25[e] | +24.2 |
| 5 | 67 | 11 | 6.25 | 0.50 | 8.75 | 1.50 | +2.50[e] | +8.3 |
| 6 | 69 | 8 | 6.50 | 1.73 | 6.75 | 1.26 | +0.25 | +0.8 |
| 7 | 72 | 16 | 4.50 | 1.00 | 4.25 | 0.96 | −0.25 | −0.8 |
| 8 | 70 | 16 | 2.50 | 0.58 | 4.75 | 0.50 | +2.25[e] | +7.5 |

[a] Four periods: baseline, lecithin only, placebo and lecithin, and placebo only.

[b] Four periods of THA and lecithin.

[c] Changes in Mini-Mental State scores were similar to cognitive changes on the Alzheimer's Disease Assessment Scale, except that patient 1 improved on the latter scale. The mean±SD change in Mini-Mental State score for the group was 1.96±2.87 ($p=0.11$, Wilcoxon signed-ranks test).

[d] Change/30×100.

[e] Greater improvement in score than expected by chance ($p=0.03$, Wilcoxon rank-sum test).

concentration during neuropsychological testing, including repeated tests, was 13.13±7.14 ng/ml, with a range of 6.5–25.0 ng/ml. The mean±SD serum choline concentration after 2 weeks of taking lecithin was 21.2±4.11 μM; for the period before lecithin was taken it was 15.5±5.31 μM ($t=2.15$, $df=6$, $p=0.05$).

Only patient 1 improved in dementia stage while taking THA and lecithin, moving from early stage 4 to late stage 3. Other functional assessments remained substantially unchanged during treatment.

Among the individual patients whose data were categorized as positive or negative (i.e., improvement or no improvement) with regard to change under the drug conditions and analyzed by calculating exact binomial probabilities, only one (patient 1) showed significant improvement ($p<0.05$; modest improvement on nine of 11 measures). When these categorical data were analyzed for the entire group by the chi-square statistic, p was <0.10, suggesting a trend toward improvement. There was no evident relationship between oral dose of THA, serum concentration of THA, and cognitive response.

The drug-titration-phase side effects have already been described. In the double-blind phase, four subjects developed elevations in SGPT and SGOT, which persisted for 3–12 weeks after cessation of THA. The elevated levels of SGPT ranged from 45 to 368 U/liter (normal range=3–36 U/liter) and of SGOT ranged from 60 to 150 U/liter (normal range=8–40 U/liter). These did not appear to be strictly dose related.

### *Outpatient Phase*

Six subjects entered and completed the outpatient phase of the protocol. Patient 3 demonstrated clinically obvious cognitive improvement during the THA and lecithin treatment, as revealed by neuropsychological tests, spouse ratings, and change in clinical stage (from stage 6 to late stage 5). Two others (patients 5 and 8) showed modest improvement on at least one major cognitive test, although clinical improvement was not as immediately obvious and no change in stage occurred. Spouse ratings did not correlate well with investigator assessments. Mini-Mental State results are summarized in table 1. The lecithin-only condition afforded no improvement over baseline or placebo-only periods. The prelecithin mean±SD serum choline concentration was 16.74±4.42 μM. After at least 2 weeks of lecithin treatment, the choline concentration was 27.26±7.32 μM ($t=4.26$, $df=5$, $p<0.01$). There were no adverse effects.

## DISCUSSION

In this study evaluating the effect of subchronic and chronic oral doses of THA and lecithin on the cognitive responses of 10 Alzheimer's disease patients, the inpatient phase revealed one patient with a mild response to treatment and a nonsignificant group trend toward improvement. However, three of the 10 subjects could not continue in the outpatient phase of the study because of substantial liver enzyme abnormalities. These treatment-limiting elevations in liver enzyme levels were not strictly related to dose or serum concentration. The outpatient phase of the study produced modest cognitive improvement in three of the six patients who completed it.

Our assessments indicate that there was cognitive improvement in about one-third of the original group of 10 patients. Of these, only one subject improved in a clinically obvious manner. For this subject, test performance was more striking than gain in daily functioning. Thus, our observations only partially support those of Summers et al. (6). However, while our findings were clearly less dramatic than those of Summers et al., THA did appear to produce a modest cognitive benefit in some of the Alzheimer's patients who were able to tolerate it. Perhaps a fraction of the Alzheimer's disease population could derive some benefit from treatment with THA.

These conclusions are limited by the size of our study group and by the advanced stage of disease in half of our subjects. Thus, the number of responders we found may not be representative of a larger, less impaired population. We believe that chronic benefits from THA are more likely to be derived by patients with relatively recent onset of the disease in whom neuronal degeneration is less severe and is predominantly cholinergic. Future pharmacologic studies may benefit from the subtyping of Alzheimer's disease.

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# $^{99m}$Tc-Hexamethylpropyleneamine Oxime Single Photon Emission CT in Poststroke Depression

**Joseph A. Schwartz, M.D., Nancy M. Speed, M.D., James M. Mountz, M.D., Ph.D., Milton D. Gross, M.D., Jack G. Modell, M.D., and David E. Kuhl, M.D.**

*In this pilot study of poststroke depression, the authors evaluated regional cerebral blood flow and depression in 14 stroke patients. Volume of ischemia was measured by two methods, which were highly correlated. Depression scores correlated with lesion volume as measured by single photon emission CT.*

(Am J Psychiatry 1990; 147:242–244)

Single photon emission computed tomography (SPECT) is a relatively new nuclear medicine technique useful in the evaluation of regional cerebral blood flow (CBF) (1–3). SPECT is now widely available: Scans can be obtained with standard rotating gamma cameras routinely used in most nuclear medicine departments. Commercially available SPECT radionuclides for the study of regional CBF include $^{123}$I-Isopropyl-iodoamphetamine and the radionuclide used in this study, $^{99m}$Tc-hexamethylpropyleneamine oxime (HM-PAO). This technique has proven application in the study of diseases of the cerebral vasculature, e.g., stroke and transient ischemic attacks (4).

When SPECT brain imaging has been used in patients with stroke, the area of decreased CBF seen is strongly correlated with the observed clinical deficits. SPECT has been shown to be more sensitive than CT in visualizing cerebral infarction, especially early in the course of the stroke. The area of decreased CBF seen on SPECT scans in most cases includes a border zone,

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The Amersham Corporation provided the radionuclide $^{99m}$Tc-hexamethylpropyleneamine oxime used in this study.

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or penumbra, of moderately decreased flow surrounding the area corresponding to the CT lesion. These findings (4, 5) suggest that stroke lesions cause CBF changes that extend outside the boundaries of the area of cell death. The border zone probably represents an area of cell injury that is sensitive to variations in blood flow.

This pilot study was conducted to explore the hypothesis that the severity of poststroke depression is related to the size of the lesion seen with SPECT. Our understanding of the relationship between poststroke depression and CT lesion characteristics, such as laterality and proximity to the frontal pole, is due largely to the contributions of Robinson and associates (6, 7). We hoped to expand on their work by exploring the utility of the SPECT imaging technique in the analysis of lesion effects in poststroke depression.

## METHOD

The participants for this study (N=14; mean±SD age=65±8 years) were recruited from a Veterans Administration rehabilitation service (10 men) and a university neurology service (two men and two women) over a 3-month period. All subjects had sufficient receptive language function for comprehension of the informed consent procedures approved by the Human Studies Committee of the University of Michigan. Patients' depression was assessed with the clinician-rated, 24-item Hamilton Rating Scale for Depression, which was completed by two psychiatrists; averaged scores were used for statistical analysis, according to the method originally described by Hamilton. When depression was defined as a Hamilton score of 18 or more, the two psychiatrists' assessments of depression were in agreement 100% of the time, giving a kappa coefficient of 1.0.

Each patient received an intravenous injection of approximately 20 mCi of HM-PAO. Imaging was performed by using the General Electric 400 AC Tomographic Gamma Camera equipped with the general all-purpose, low-energy, parallel hole collimator. Image reconstruction was performed with a Siemens Microdelta Computer. A total of 128 angular views over 360 degrees was obtained beginning 15 minutes after the injection. The time per stop was 12 seconds. Total acquisition time was approximately 45 minutes, yielding between 5 and 8 million counts per SPECT image. Image reconstruction was performed by using a Butterworth filter (order=5, frequency cutoff=0.35), and the images were attenuation corrected.

SPECT region of interest analyses for quantifying the stroke lesion were performed independently by two investigators using different techniques.

Method 1: One investigator outlined the area in each slice that had as its margin 25% less blood flow than the contralateral side. The number of pixels inside this margin were counted and summed for the slices demonstrating that degree of regional CBF defect. Each pixel is a square measuring 0.625 cm. The slice thickness on reconstruction is also 0.625 cm.

Method 2 (8): The other investigator drew a region of interest that extended beyond the margin of the lesion. The number of pixels (N) and average counts per pixel (Cts/P) were determined for the region containing the lesion (D) and for the corresponding identical region of interest on the contralateral cerebral hemisphere (C). A hypothetical volume of complete loss of blood flow was then obtained by the equation:

$$\text{Volume} = \frac{\text{Cts/P(C)} - \text{Cts/P(D)}}{\text{Cts/P(C)}} * N * \frac{\text{Volume}}{\text{pixel}}$$

Linear regression analysis was used to determine the relationship between Hamilton depression scores and three factors: SPECT lesion volumes measured by methods 1 and 2, age, and time since stroke. Linear regression analysis also was used to evaluate the correspondence between lesion volumes measured by methods 1 and 2.

## RESULTS

Hamilton depression scores, SPECT lesion volumes (calculated as described in Method), and CT lesion locations are shown in table 1. We found that depression scores were correlated with SPECT lesion volumes (linear regression, method 1: r=0.56, df=12, $p<0.05$; method 2: r=0.54, df=12, $p<0.05$). SPECT lesion volumes defined by the two methods were very highly correlated (r=0.97, df=12, $p<0.001$). Lesions visualized by CT and SPECT were localized to the same regions in all cases.

Patients' ages and weeks since stroke are also shown in table 1. There was no significant relationship between depression ratings and these two independent variables by linear regression analysis (age: r=0.09, df=12, p=0.80; time: r=0.14, df=12, p=0.60).

## DISCUSSION

This pilot study shows an association between poststroke depression and the size of the cerebral lesion as measured by HM-PAO SPECT. Our findings are consistent with the preliminary abstract of Yamaguchi and colleagues (9), in which they reported a correlation between the size of the blood flow defect measured by xenon inhalation and the severity of depression in 114 depressed stroke patients. They also scanned 38 of these patients a second time and noted a highly significant correlation between increases in regional CBF in the temporal regions bilaterally and reduction in depression in the time between scans.

This pilot work suggests that SPECT may be useful in studying poststroke depression. Further work is needed with larger samples to evaluate the relation-

**TABLE 1. Hamilton Depression Scores and Lesion Characteristics of 14 Stroke Patients**

| Patient | Hamilton Score | Lesion Volume Measured With SPECT: Method 1 (pixels) | Lesion Volume Measured With SPECT: Method 2 ($\text{cm}^3$) | Weeks Since Stroke | Age (years) | Location of Lesion[a] |
|---|---|---|---|---|---|---|
| 1 | 1 | 0 | 15.0 | 4 | 66 | LT-P |
| 2 | 4 | 0 | 9.3 | 4 | 54 | RT-F,P |
| 3 | 8 | 0 | 0.0 | 24 | 72 | RT-F |
| 4 | 10 | 0 | 4.6 | 250 | 70 | Bi-BG |
| 5 | 13 | 723 | 67.0 | 15 | 64 | LT-F,T,P,O |
| 6 | 15 | 540 | 37.0 | 14 | 64 | Bi[b] |
| 7 | 15 | 610 | 38.0 | 30 | 65 | Bi-T |
| 8 | 17 | 0 | 0.3 | 250 | 66 | Bi-F |
| 9 | 18 | 0 | 2.7 | 2 | 44 | LT-P |
| 10 | 21 | 312 | 47.0 | 8 | 84 | Bi-T |
| 11 | 27 | 963 | 64.0 | 60 | 62 | LT-T,P,O |
| 12 | 28 | 192 | 43.0 | 13 | 65 | LT-O |
| 13 | 30 | 132 | 6.6 | 35 | 68 | Bi-F |
| 14 | 33 | 2,718 | 343.0 | 8 | 69 | RT-F,T,P,O |

[a] LT=left hemisphere, P=parietal lobe, RT=right hemisphere, F=frontal lobe, BI=bilateral, BG=basal ganglia, T=temporal lobe, O=occipital lobe.

[b] Right frontoparietal bleeding with bilateral ventricular blood on CT.

ships between SPECT lesion location and depression, in order to compare the SPECT findings with the CT findings of Robinson and colleagues.

We also found a high degree of correlation between our two measurement methods, suggesting that defects in SPECT images can be reliably quantified. Early standardization of methods for measuring image features for psychiatric investigations will be crucial for the comparison of data between centers involved in SPECT research. We recommend the use of method 2 because it is simple to perform and easily replicated, requiring only that the region of interest is drawn beyond the region of visible count defect. In addition, it yields a defect volume of hypothetical zero blood flow (cubic centimeters) that can be appropriately compared with the low attenuation region visualized on CT.

SPECT may have clinical utility in the assessment of poststroke depression. Patterns of regional blood flow impairment may be shown to predict depression, spontaneous recovery, and need for antidepressant medications. Poststroke syndromes are only one of the many common problems that involve both brain injury and emotional disability. SPECT shows promise as a tool for the investigation of these problems.

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# Predicting Compliance With Command Hallucinations

John Junginger, Ph.D.

*Of 44 patients who experienced command hallucinations, those with hallucination-related delusions and hallucinatory voices they could identify were more likely to comply with the commands. The danger of the behaviors specified by the hallucinations did not appear to be a factor in compliance.*

(Am J Psychiatry 1990; 147:245–247)

Potentially the most disruptive verbal hallucinations are those that command the subject to behave in a specific manner. Although some hallucinatory commands, such as orders to take out the garbage or clean the house, are harmless, there is evidence that many of these hallucinations are dangerous. Hellerstein et al. (1), for example, found that 40 (69.0%) of 58 patients experiencing command hallucinations reported being commanded to commit suicide, homicide, or injury to self or others.

However, research thus far has suggested that command hallucinations have little clinical relevance. In a study of the diagnostic significance of hallucinations, Goodwin et al. (2) found that subjects who experienced command hallucinations generally ignored them and that none of the subjects had committed dangerous or destructive acts in response. In addition, Hellerstein et al. (1) reported no significant differences in assaultive acts between subjects with and without command hallucinations, and Breier and Astrachan (3) found no history of command hallucinations in 20 schizophrenic subjects who had committed suicide.

The results of these studies are contrary to the clinical impressions of a number of authors and, presumably, mental health professionals. In a study of inpatient violence, for example, Yesavage (4) claimed that command hallucinations were correlated with dangerous acts because patients unexpectedly acted on the commands. Unfortunately, the evidence supporting this conclusion was not reported. Psychiatric texts also perpetuate what some have suggested is clinical folklore (1), the belief that command hallucinations are dangerous. They warn that command hallucinations may "lead to direct and dangerous action" (5) and that a patient "may kill himself simply in response to relentless commands he is receiving from his hallucinatory voices" (6).

This disparity between clinical impression and research is puzzling. Apparently, what clinicians believe to be true about command hallucinations is difficult to confirm empirically. There may be a number of reasons for this discrepancy. Hellerstein et al. (1), for example, speculated that the population of patients with command hallucinations as a whole are not at risk for dangerous behavior but that as-of-yet undefined subgroups may be.

A potentially more productive focus for research might be the identification of variables related to compliance with command hallucinations. Such a strategy directs attention to compliance; determining the relative dangerousness of patients with and without command hallucinations adds little to the prediction of dangerous behavior on an individual basis.

We can also ask about the relative levels of compliance with dangerous and harmless commands. It may be that compliance is determined not only by patient characteristics, but also by the danger of the behavior specified by the hallucination. It seems reasonable to assume that patients are more likely to comply with harmless commands than with dangerous ones. As a group, therefore, these patients may be no more at risk for dangerous behavior than patients who do not experience command hallucinations.

The purpose of the present exploratory study was to identify variables that differentiated patients who complied with their hallucinatory commands from those who did not. It was hypothesized that the danger of the behavior specified by the command would be one factor in compliance—that is, patients would be less likely to comply with dangerous commands.

## METHOD

The subjects were 51 psychiatric inpatients and outpatients. Each of these subjects had reported in a psychiatric interview that during the most recent verbal hallucination a voice had instructed or commanded him or her to behave in a specific manner.

Psychiatric diagnoses were assigned on the basis of

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information obtained in a semistructured psychiatric interview and hospital chart review and were made according to *DSM-III-R* criteria. Twelve (46.2%) of the 26 subjects diagnosed as schizophrenic and eight (80.0%) of the 10 subjects diagnosed as having mood disorder were independently assessed with the Diagnostic Interview Schedule (DIS) (7). These independent assessments showed 83.3% agreement with the study diagnoses of schizophrenia (two schizophrenic subjects were diagnosed as having atypical depression according to the DIS) and 87.5% agreement with the study diagnoses of mood disorder (one mood disorder subject was diagnosed as having schizoaffective disorder according to the DIS). Diagnoses other than schizophrenia and mood disorder were not independently assessed.

During the psychiatric interview, each subject was asked to describe verbatim what the voice(s) said during the most recent command hallucination. The subjects were asked if and how they complied and whether they recognized the voices. Any subject who reported current or past delusional beliefs during the interview was asked to describe the most recent prominent delusion in detail and provide any evidence he or she had for the belief.

For each subject, potential compliance with a hallucinatory command was judged to be either dangerous or harmless. The most frequent dangerous commands were orders to take an overdose of medication and commands to inflict physical harm on self or others; harmless commands included commands to do the laundry, turn on the television, and so on. A subject was judged to have complied if he or she reported specific behaviors and the intention to carry out the command.

## RESULTS

Twenty (39.2%) of the 51 subjects with command hallucinations reported that they had complied with the commands. Twenty-four subjects (47.1%) reported that they did not comply, and seven (13.7%) could not recall.

As shown in table 1, the danger of complying with a hallucinatory command appeared to have less impact on actual compliance than might be expected. This was true even when taking into consideration the seven subjects who reported they could not recall whether they had complied. These seven subjects were dropped from further analyses.

A visual inspection of the data appeared to show that four variables were related to compliance: 1) recognition of the hallucinatory voice, 2) the presence of a delusional belief for which the subject offered as evidence aspects of his or her verbal hallucination—that is, a hallucination-related delusion (the presence of delusions in general was not related to compliance), 3) black race, and 4) diagnosis of schizophrenia. Recognition of the hallucinatory voice and hallucination-related delusions appeared to have the strongest relationship with compliance (see table 1).

**TABLE 1. Relation of Compliance With Command Hallucinations to Danger of Behavior Specified, Hallucination-Related Delusions, and Recognition of Hallucinatory Voices**

| Variable | Compliance: Yes (N=20) | Compliance: No (N=24) | Compliance: Unknown (N=7) | Total: N | Total: % |
|---|---|---|---|---|---|
| Type of behavior specified (N=51) | | | | | |
| Dangerous | 8 | 12 | 0 | 20 | 39.2 |
| Harmless | 12 | 12 | 7 | 31 | 60.8 |
| Hallucination-related delusion (N=44) | | | | | |
| Present | 14 | 8 | — | 22 | 50.0 |
| Absent | 6 | 16 | — | 22 | 50.0 |
| Recognition of hallucinatory voice (N=44) | | | | | |
| Present | 14 | 8 | — | 22 | 50.0 |
| Absent | 6 | 16 | — | 22 | 50.0 |

Variables appearing to have a relationship to compliance were coded at two levels to be entered into a multiple regression analysis. Diagnosis was designated as either schizophrenic (N=23) or nonschizophrenic (N=21), and recognition of the hallucinatory voice was divided into two more specific variables, "familiar" and "human." "Familiar" referred to whether the subject could identify or name the source of the voice. The variable "human" referred to whether the voice was identified as human (friends, relatives, unknown) or nonhuman (God or the devil).

The five variables and compliance were entered into a regression analysis, with compliance as the dependent variable. The independent variables were entered in a stepwise, forward manner. The F-to-enter and F-to-remove values were set at 1.

Three of the five variables (hallucination-related delusion, familiar, race) explained 23% of the variance in compliance. After adjustment for shrinkage, these three variables accounted for approximately 18% of the population variance for compliance ($F=4.05$, df=3, 40, $p<0.01$). Significant increases in explained variance were provided by hallucination-related delusion ($F=6.95$, df=3, 40, $p<0.01$) and, to a lesser extent, familiar ($F=3.97$, df=3, 40, $p<0.05$). Subjects who reported hallucination-related delusions and could identify the voices were more likely to comply with hallucinatory commands—regardless of the danger. These two attributes were present in 11 (55.0%) of the 20 subjects who complied but only three (12.5%) of the 24 subjects who did not comply. Conversely, only three (15.0%) of the 20 subjects who complied neither could identify their voices nor had hallucination-related delusions, but this was the status of 11 (45.8%) of the subjects who did not comply. Potentially more important for the prediction of dangerous behavior was the finding that five (62.5%) of eight subjects reporting compliance with dangerous commands could identify their voices and had hallucination-related delusions. However, this was the status of only one (8.3%) of 12 subjects who did not comply with dangerous commands.

## DISCUSSION

The relatively high rate of compliance with hallucinatory commands found in this study differs noticeably from the rates in the studies cited earlier (1–3). The high rate of compliance found here may be due to a recall bias on the part of the subjects, who were more likely to recall command hallucinations with which they had complied than those with which they had not. This may be particularly true of dangerous commands. For example, the seven subjects in the present study who could not recall whether they had complied with their hallucinations all reported harmless commands. This may indicate that both noncompliance and harmless commands were underreported.

This explanation, however, cannot account for the differences between these findings and those reported by Goodwin et al. (2), who apparently used similar methods. Goodwin et al. reported that none of their subjects committed dangerous acts because of their command hallucinations. This certainly was not the case in the present study; eight (40.0%) of the 20 subjects experiencing dangerous commands complied. One possible explanation for this discrepancy is that the present study assessed the most recent verbal hallucinations reported by the subjects, while the Goodwin et al. data were not limited to recent experience; it is unclear how this sampling difference might have influenced the results.

The results of the present study suggest a number of interpretations. Identification of voices and hallucination-related delusions may simply indicate more severe psychotic disturbance—so severe, in fact, that rational considerations such as the danger of complying with hallucinatory commands apparently are ignored. Thus, collateral measures of certain aspects of hallucinatory experience, such as the frequency of hallucinations, also may be related to compliance.

Other results suggest that the variables predicting compliance are more specific than simple level of psychotic disturbance. As already reported, hallucination-related delusions but not delusions in general were related to compliance. This finding seems to support more specific interpretations of the relationship between symptom attributes and compliance.

Identification of voices and hallucination-related delusions may indicate a more systematized or consistent distortion of reality. The hallucinatory experiences of subjects with these symptom attributes may seem more real, or at least more consistent with their distorted sense of reality, and the patient therefore may be more likely to comply; that is, compliance may be easier as questions about psychotic experiences (e.g., Who's talking to me and why?) are resolved.

The present study is exploratory, and its results should be interpreted cautiously. Nevertheless, the results are consistent with reported clinical experience and suggest that patients who have hallucination-related delusions and who can identify the voices are at risk for dangerous behavior when their hallucinations command it.

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# Book Forum

## Nancy C. Andreasen, M.D., Ph.D., Editor

## SCHIZOPHRENIA

**Schizophrenia: Treatment, Process, Outcome,** *by Thomas H. McGlashan, M.D., and Christopher J. Keats, M.D. Washington, D.C., American Psychiatric Press, 1989, 195 pp., $28.00.*

This book reports on the psychotherapeutic treatment at Chestnut Lodge of four patients selected on the basis of outcome, two favorable and two unfavorable. The goal was to relate outcome to what was known of the treatments, with the hope of improving psychotherapy. The report is modest and sensible. There are no startling findings. We think that most students of schizophrenia will find it a clinically truthful document. We also suspect, along with the authors, that the findings, even though from some 20 years ago (to permit a lengthy follow-up), have not been superseded by present-day findings in character or outcome.

Read together with Robert Wallerstein's review of the Menninger Clinic study of borderline patients (1), this book leads to the conclusion that the interpretative psychotherapies seem more important than interpretations or clarifications.

The book makes it clear that much was unknown to the clinicians about most of these patients—even in the setting of close and intense observation and discussion that Chestnut Lodge provides. Both schizophrenia and human beings remain very mysterious. The authors work hard to penetrate these mysteries, to understand the patients' needs and how to meet them. We agree with the authors that the development of both interpersonal and existential psychiatry (including self psychology) has importantly advanced our understanding of these needs.

The authors suggest that whatever gains can be made in the fight against the symptoms of schizophrenia, important difficulties of character and social situation remain. Psychological treatments continue to occupy the central place in the fight against these difficulties.

Of course, it is not known how much difference even the most specific and flexible psychotherapy can make. One importance of this book is its demonstration that extraordinary gains occur (possibly related to psychological treatment and sometimes without medication) and that the pursuit of effective psychotherapies is an important task in the treatment of all patients.

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**Handbook of Schizophrenia, vol. 1: The Neurology of Schizophrenia,** *edited by Henry A. Nasrallah and Daniel R. Weinberger; Henry A. Nasrallah, editor-in-chief. New York, Elsevier, 1986, 406 pp., $92.50.*

To a surprising extent, many of the currently debated areas in schizophrenia research (possible neuropathological localization, disease progression, and genetic and perinatal contributions, to name only a few) are found as clearly stated conjectures in the writings of Kraepelin and Bleuler. What has not existed until recently, however, are the scientific means to test these hypotheses rigorously.

There has been a steady push forward into the study of brain abnormalities in schizophrenia, motivated in large part by advances in brain imaging and neurochemistry. As a result, there is a need for a book or a series of books to integrate this surge of new information in a critical manner and also to construct a series of intelligible, theoretical frameworks into which the new observations can be placed. Ideally, such a book would complete the dialectic by reordering the particular observations from astride the overall framework and by generating novel testable hypotheses.

The current volume, dealing with the neurology of schizophrenia, is the first in a series that spans neuropsychology and psychophysiology, neurochemistry and neuropharmacology, epidemiology and genetics, and psychosocial therapies. To a creditable extent, this first volume succeeds in its objective, which is to provide a broad-ranging and thorough documentation of recent scientific evidence for schizophrenia as a brain disease. Its 18 chapters deal with a wide variety of schizophrenia-related topics, including the neurological examination, differential diagnosis, associated motor abnormalities, neurology of tardive dyskinesia, EEG and evoked potential studies, neuropsychological approaches to the syndrome, hemispheric asymmetries, and a review of evidence implicating various brain regions. Additional chapters review X-ray CT and magnetic resonance imaging of the brain, computerized mapping of electrophysiological data, cerebral blood flow and positron emission tomography studies, anatomical neuropathology, post-mortem neurochemistry, viral hypotheses, neuroimmunology, and neurodevelopmental hypotheses of pathogenesis. A strong range of authors is represented, including many current and former intramural researchers from the National Institute of Mental Health.

Several of the chapters, including those coauthored by Weinberger, examining neuropathology, X-ray CT, and cerebral blood flow studies are excellent, as is the review of post-mortem neurochemical studies by Kleinman. Between them, the two editors of this volume contribute substantially to the chapters: Henry Nasrallah is an author or coauthor of three plus the introduction, and Daniel Weinberger contributes as an author or coauthor to eight of the 18 chapters.

On the down side, this volume is not inexpensive. Some of the chapters review a large amount of information without the full critical discussion one would expect in terms of sorting out good from bad studies, synthesizing the former for the reader, and formulating new hypotheses. The final chapter, by Weinberger, clearly succeeds in these goals, however. As a relatively minor point, the indexing, which is nonalphabetized and includes only the first page number of citations, is somewhat frustrating.

In summary, Nasrallah and Weinberger have edited and contributed to a high-quality, comprehensive book that contains something for everyone—beginning students, focused schizophrenia researchers, and clinical psychiatrists with a general interest in schizophrenia. This is an excellent sourcebook with more breadth than the average conference proceedings yet with sufficient scope to avoid being superspecialized. A volume such as this is helpful both to summarize what we know and to help formulate directions for further study. The editors have managed by and large to avoid overlap between chapters. I have been recommending this book to psychiatry residents and research postdoctoral research students for some time; it is definitely a useful addition to the schizophrenia literature.

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## HOSPITAL AND COMMUNITY PSYCHIATRY

**Modern Hospital Psychiatry,** *edited by John R. Lion, Wolfe N. Adler, and William L. Webb, Jr. New York, W.W. Norton & Co., 1988, 415 pp., $39.95.*

After Rome declined and fell, Byzantium held on for 1,058 more years of net decadence. It had 107 emperors, 67 of whom were deposed or died unnaturally. Byzantine politics is what *Modern Hospital Psychiatry* is about.

There were several sorts of "nonmodern" psychiatric hospitals. One example was "bedlam," which protected emerging urban sensibilities from contact with the seriously mentally ill. The accommodations were basic, and milieu therapy alone was provided. A second sort was the luxury spa, where the wealthy could pamper their collective neurasthenia at leisure. The former have been decimated by neuroleptics, deinstitutionalization, and site visitors; the latter by the decline of the ruling classes. Both are trying to transform themselves into the modern psychiatric hospital, a development aided initially by relatively liberal funding for health care. More recently, funding has declined. Diagnosis-related groups, health maintenance organizations, length-of-stay guidelines, tort lawyers, Health Care Financing Administration auditors, and many others are imposing smothering paperwork burdens as they strangle our funds.

*Modern Hospital Psychiatry* is not a manual of hospital practice. It is more a series of essays on how things are. The various authors work in all sorts of modern psychiatric hospitals and health care disciplines. The book contains numerous short clinical case vignettes.

The book also describes Byzantine politics: Milieu psychotherapists who find the medical model antithetical but tolerate physicians for the occasional patient who they decide needs ECT or who has a "biological" (drug-induced) depression. A psychotherapist who tolerates individual psychodynamic therapy but argues that any discipline could deliver it. Complaints of cognitive-behavioral therapists about psychoanalysts "impervious to rational persuasion or citations of relevant empirical literature." A community meeting that votes to increase the dose of a troublesome fellow client's lithium. Nostalgia for the brief paradisiacal days of 1972, the year McGovern lost, when the Federal Employees Health Benefits Program briefly decided to cover 365 inpatient days (it later rescinded the decision). Complaints about the "arbitrary limits" government agencies now impose on lengths of stay. The elaborate process by which one can assess the individual needs and strengths of each patient, described verbosely and translated into initial target behaviors, short-term objectives, and long-term goals, with the result that the patient is assigned to the usual therapy groups and recreational activities. Each discipline scratching for a larger part of a declining whole.

Until recently, hospital psychiatrists were respected. Such were the founders of APA. This group has diminished in size and influence, however, leaving many of Byzantium's remnants to teams and committees. A few great leaders, like Justinian, Leo III, Basil II, Lion, Adler, and Webb, have remained to delay or even temporarily reverse the empire's decline. Is it time to take the hospitals back, or do they deserve our continued disdainful avoidance? This book accurately reflects the current conditions of our hospitals, giving equal treatment to ancillary personnel and to scholarly medical directors.

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**Community Mental Health: Principles and Practice,** *by Loren H. Mosher and Lorenzo Burti. New York, W.W. Norton & Co., 1989, $35.95.*

Although our knowledge of the neurobiological underpinnings and psychosocial determinants of serious mental illness has exploded exponentially, it is bitterly ironic that our ability (or willingness) to translate this knowledge into care and caregiving systems for most of those afflicted has barely seemed to move at all. Mosher and Burti believe that much more is known about effective community-based treatment than is currently widely implemented. They present a sweeping and personal history of the community mental health movement, an outline of what is wrong with mental health services as currently configured, and a comprehensive humanistic vision of what ought to be done about it. By necessity, this tall order is filled in a book ambitious in scope, provocative in tone, and radical in outlook.

Working mostly in public systems, Mosher in the United States and Burti in Italy have accrued extensive hands-on experience in the design, operation, and evaluation of community-based alternatives to psychiatric hospitalization. Their basic position is that although 70% of mental health expenditures are still consumed by costly inpatient services, alternative models of home-based and crisis residential care of at least equal efficacy already exist and might better serve the needs of most (but not all) individuals currently treated in hospitals. Current National Institute of Mental Health initiatives notwithstanding (1), they argue that these models are underused not for scientific but for essentially economic and sociopolitical reasons.

The heart of this book is a clinical posture that is practical, respectful, and problem oriented. Principles, priorities, attitudes, and values seen as key ingredients in the provision of effective mental health services are articulated and then elaborated in a "how to" manner into clinical interventions and organizational structures. Reminiscent of Sullivan (2) but more widely accessible, the chapters on psychosocial interviewing provide an elegant and jargon-free overview that would serve well as core reading for trainees in all mental health disciplines. Later chapters extend this essentially clinical perspective into the realm of the administrative organization, staffing, maintenance, and evaluation of an innovative alternative service system. The second half of the book is a collection of detailed case studies of successful community-based programs for patients with chronic mental illness in both Italy and the United States. This includes a fascinating social history of the highly politicized reform movement in Italy that culminated in a legislatively mandated halt to new admissions to state hospitals. Among innovative U.S. programs described in depth are comprehensive systems operating in both relatively resource-rich (Dane County, Wis., and Boulder, Colo.) and impoverished (Morrisania, South Bronx, N.Y.) settings.

Mosher and Burti may find their clinical perspectives embraced by a wide range of unexpected bedfellows as employers and insurance carriers become increasingly concerned over the rising cost of mental health care. It is likely that the next decade will witness the wholesale application of the principles and practices of community mental health in the private sector. Limitations in access to inpatient services imposed by managed care, concurrent review, and other cost-saving schemes may well eventuate in a new deinstitutionalization of the middle class. This book provides one of the few available blueprints for preserving and maximizing quality across both private and public contexts in a future where concern with cost will gain in urgency.

A word of warning: this is no dull academic treatise. As Luc Ciompi notes in his laudatory preface, this book is provocative; most readers will disagree with certain points or propositions, at times finding the authors too radical, outrageous, or extreme. Those with a weak stomach for polemics are urged to steer clear. Unrestrained but ecumenical in their criticisms, there is something here to offend nearly everyone. Those (like myself) who found the raw social commentary of Reich's *Listen Little Man* (3) and Laing's *The Politics of Experience* (4) stimulating and thought provoking rather than offensive will be similarly gratified here.

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**Costs and Effects of Managing Chronic Psychotic Patients,** *edited by Detlof Schwefel, Herbert Zöllner, and Peter Potthoff. New York, Springer-Verlag New York, 1988, 252 pp., $77.60 (paper).*

The World Health Organization (WHO) Regional Office in Europe has led in the development of research on the economics of care for the chronically mentally ill. Since the early 1970s, this WHO group has encouraged studies across national boundaries to compare at least two or more strategies that emphasize a variety of inpatient or outpatient care modalities to manage patients with chronic psychosis. The group considered but decided against a fully coordinated multinational, multicenter study based on mutually agreed study protocols and has instead stimulated a variety of different research approaches and projects across Europe. This volume is a compilation of descriptions of these projects, initially presented at a conference held in Munich in December 1985.

There are 15 papers presented in all. In the first two comprehensive background papers the authors develop terms of reference for all the studies being pursued. The next chapters describe approaches and results in Ireland, Greece, the United States, Denmark, Spain, Canada, The Netherlands, Italy, England, Scotland, Switzerland, and West Germany. They are a potpourri of cost-benefit and cost-effectiveness studies, outcome studies with costs as one variable, and methodological approaches that use an interdisciplinary approach involving economists, psychiatrists, social scientists, and government administrators. It is, therefore, an extremely interesting and rich compilation of studies on the interface of economics and psychiatric care for a major public health problem—the treatment and management of chronic psychosis.

The editors state in the preface, "It is our prejudice that a bundle of wild flowers is nicer than a bunch of mechanically produced or even cloned tulips." They say this to justify the varied nature of the papers contained in this book, and certainly some of the papers are more beautifully developed and richer than others. The studies reported from Canada and Italy are especially valuable from the perspective of choosing cost-effective community versus institutional approaches for patients and for especially recommending approaches that emphasize continuity of care.

A theme that pervades every chapter in this book is the effort to clarify treatment and rehabilitative choices for dealing with illness and disability which have an impact on many aspects of individual and family functioning. These choices are described through an economic analysis that is potentially helpful both to the clinician decision maker and to the government official in charge of paying for such care. In the United States, with our extraordinary patchwork quilt of financing and support, such decision making remains more difficult than it is in European countries with national health systems. Our system relies on the competing advocacies of groups vitally concerned with social welfare, tax policy, or treatment opportunities. The chapter by Drs. Frank, Lave, and Goldman from the United States is a very useful summary of the confusion in methods of financing care for the chronically mentally ill here. These authors emphasize the current trend, which moves treatment and financing decisions from provider groups to the patients and families themselves. This is described as a shift from "supply-side" programs to "demand-side" programs. The authors caution strongly that this shift puts the most vulnerable chronically ill patients at risk to adverse provider responses. They promote a "voucher case manager approach," which tries to combine both demand- and supply-side incentives, but caution that more research is needed before it is implemented on a widespread basis.

It is clear that we can learn a good deal from the experience of other Western countries, and the WHO working group should be commended for its decade-long devotion to these studies in services research. Concerned clinicians and policy makers in this country will benefit from reading the studies contained in this volume.

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## THE HOMELESS MENTALLY ILL

**Nowhere to Go: The Tragic Odyssey of the Homeless Mentally Ill,** *by E. Fuller Torrey, M.D. New York, Harper & Row, 1988, 247 pp., $18.95.*

After the AIDS epidemic, the plight of the homeless mentally ill is the most urgent public health problem in the United States. In the last quarter century, the shift of neglect of the severely mentally ill from large custodial institutions to mean, uncaring streets underscores the manmade nature of a social policy disaster. The current epidemic of hallucinating and delusional nomads in our cities is a tragic story. It is told in this book by Dr. Torrey as a political and moral tale in a style reminiscent of muckraking journalists of the past. Dr. Torrey indicts almost everyone—liberals and conservatives, Democrats and Republicans, public health officials, federal and state politicians, psychiatrists, the mental health professions, and the various lobbyists and bureaucrats who have championed the mental health movement for the past 40 years. There is plenty of blame to go around. The writing is clear and lively and to the point and, like its predecessor, *The Shame of the States* by Albert Deutsch (1), leads to a call for action. But will we just repeat the mistakes of the past in well-intentioned efforts at reform as if we had total amnesia for a history that has been marked by overpromise, political opportunism, professional apathy, and societal neglect?

A basic lesson of this book is that good intentions are not enough; without research, hardheaded priority setting, and purposeful financing, we will fail again. Today's failures include the homeless mentally ill, jails filled with the mentally ill, woefully inadequate aftercare and community programs, more incidents of violence in society committed by individuals with mental illness, and reinstitutionalization in private nursing and board and care homes. Dr. Torrey describes in great detail the plight of the severely and seriously mentally ill in all of these settings, although he touches too lightly on problems in nursing home settings, perhaps because they are not so obvious and painful as the situations that we can see daily on the grates of our large cities.

This book is not perfect by a long shot. It is a selective history with polemical and sarcastic aspects that detract from the analysis, and parts are biased by the author's strongly held views. For example, in blaming the community mental health centers program for failing to serve the chronically mentally ill Dr. Torrey omits large chunks of the history of this program. There was overpromise in the expectation that these programs would somehow take over the role of the state mental hospital, and this was matched by overpromises in other areas, including preventing mental illness and treating diverse special populations such as the chemically dependent, the elderly, children and adolescents, and rape victims. Indeed, community mental health centers were expected to take care of all human misery. These expectations were built into the legislative process in order to achieve congressional passage. In areas where large numbers of patients were discharged from state hospitals, the mental health centers were easily overwhelmed. The response of the federal government in the 1970s was to decrease the funding and increase the regulations. I believe that if the financial incentives had been there, many of the mental health centers would have been more a part of the solution than part of the problem. As it stood, however, the saga of shifting the cost of care for these patients to other sectors and systems undermined the planning of any rational treatment and follow-through for these patients. The mental health centers, unfortunately, were no exception to the overpromise of other programs in the 1960s. In another area, Dr. Torrey takes some gratuitous swipes at the psychoanalytic psychotherapy movement in the United States, which bears indirectly on the public health crisis we face today.

At points, I have difficulty with Dr. Torrey's use of numbers and broad-based generalizations. Despite these defects, however, this is the best book I've read on this troubled subject, and the recommendations at the end can only be applauded and underscored. These include the need to set our priorities right and focus on the seriously mentally ill. Dr. Torrey presents the case that psychiatrists must treat individuals with serious mental illness. He argues for the fixing of government responsibility for the seriously mentally ill at the state or local level. He calls for housing improvements for this population. He cries for civil liberty reform so that laws regarding the mentally ill can be changed to ensure that those who need treatment can be treated. Finally, he argues that research on the causes, treatment, and rehabilitation of serious mental illness must increase substantially. He states that federal leadership is key in this last area. I would argue further that federal leadership is important not only to fund research; without such support state and local governments will not have the funding or technical capacity to develop a system and stick clearly to the priorities. The Community Support Program of the National Institute of Mental Health (NIMH) is one example of federal leadership that has influenced the organization, financing, and delivery of psychiatric services for the chronically mentally ill at the state and local level, and there are other NIMH demonstration and research programs that are developing ways to influence state programs to improve their service systems. Further, Social Security, which is essential to providing medical and social support services for this population, should be reformed and targeted to work through state and local agencies to provide coordinated opportunities for treatment and support in the community. The federal government's presence is important at the local and state level in the face of the public outcry that can swing the pendulum back to wholesale reinstitutionalization in the large snake pits of the past.

Dr. Torrey has been a controversial figure in U.S. psychiatry. He reserves some of his sharpest criticism for the profession itself. It is interesting to note that psychiatrists are responding to the moral challenge presented in this book. I believe that the remedicalization of the profession, the focus on the seriously ill, the research breakthroughs, improvements in financing, and the greater professional rewards will continue to lead more psychiatrists to treat the seriously mentally ill and to provide psychiatric leadership to the systems of care that are responsible for them.

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**Homelessness, Health, and Human Needs,** *by the Institute of Medicine Committee on Health Care for Homeless People. Washington, D.C., National Academy Press, 1988, 227 pp., $29.95; $19.95 (paper).*

**Homeless Families,** *by George Thorman. Springfield, Ill., Charles C Thomas, 1988, 142 pp., $29.95.*

"We stay in places where you're afraid to fall asleep. We eat food nobody else wants. We spend all day on the street walkin' with no place to go. People look at us like we're trash." So opens Thorman's book on homeless families. Why has this happened? Deinstitutionalization of the 1960s and 1970s poured the psychiatrically ill into single-room-occupancy housing. Since 1970, however, there has been a national decline in such housing from two million units to one million. Low-cost housing has declined at the rate of about 300,000 units annually since 1980. Although economists believe that 30% of one's income should go toward housing costs, for three out of ten low-income renters it exceeds 70%. Hence, the most vulnerable citizens, the psychiatrically ill, have swelled the ranks of the homeless in the United States to the point that two out of three of the homeless are mentally ill (half are substance abusers). There are twice as many psychiatrically ill on the streets as there are in public psychiatric hospitals (1, p. 9).

Although the state's public psychiatric hospitals were responsible for the psychiatrically ill 30 years ago, today that responsibility is shared with federal, city, and county governments. Although psychiatric institutions were responsible for the public psychiatric patient, today that responsibility is shared with mental health clinics, the courts, the legislatures, and other public agencies. Responsibility has become diffuse.

These two books provide a review of the problem and make recommendations. The Institute of Medicine provides the history and the data. Thorman has us meet homeless families. They both make many recommendations that are largely within the shadows of the 1984 recommendations of APA (2).

Both books avoid attacking psychiatrists, but as one reads the Institute of Medicine's data and Thorman's case histories, it occurs that psychiatrists had a chance to prevent some homelessness. But we followed the law, agreed with the hypothesis that institutions were bad, and let the patients join the abandoned in the streets. Missing for the public psychiatric administrator have been any ethical guidelines as to the degree to which we are responsible for the patient regardless of laws and regulations, or at least a standard of how to represent the psychiatric patient's best interest.

What to do? We can agree with both books and blame Reagan, but that doesn't help the homeless. These books make more than 50 recommendations. Too many to be heard. And the total costs of implementing all of these recommendations would be enormous. Although these books stress the basic need for housing, they also ask that many other needed services for the homeless be institutionalized.

What to do? APA's task force report said, "Persons with severe chronic mental illnesses are among the nation's most vulnerable citizens and are unable to advocate for their own needs. No task for mental health professionals is more important than publicly championing the needs of these patients" (2, p. 276). True, but what priority should we champion? These two books make it clear that we got into abandoning the psychiatrically ill by adopting policies that had not been tested. Richard Jed Wyatt and Evan G. DeRenzo summarized the problem with the phrase "scienceless to homeless" (3). Our priority should be to test policies to find out what works, to give policy a sound empirical foundation for actions intended to serve the psychiatrically ill.

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## AIDS

**Psychological, Neuropsychiatric, and Substance Abuse Aspects of AIDS,** *edited by T. Peter Bridge, Allan E. Mirsky, and Frederick K. Goodwin. New York, Raven Press, 1988, 261 pp., $30.00.*

This volume, published as part of the Advances in Psychopharmacology series, presents a wide-ranging collection of articles addressing topics broadly encompassed within the fields of the behavioral and biological neurosciences related to acquired immune deficiency syndrome (AIDS) and human immunodeficiency virus (HIV). As we approach the second decade of experience with AIDS, volumes addressing more and more specialized areas of interest are being published in a number of disciplines, and this book is representative of such "second generation" works.

The book consists of 23 chapters about diverse subjects written from varying perspectives. Some, such as T. Peter Bridge's "AIDS and HIV CNS Disease: A Neuropsychiatric Disorder," are helpful general summaries of available knowledge about domains of AIDS-related information. Several others provide discussions of specific and highly circumscribed topics, such as "Characterization of Interleukin-1 Receptors in Brain" and "Synthetic Peptides in the Study of the Interaction of Rabies Virus and the Acetylcholine Receptor." Some chapters, such as David Ostrow's "Models for Understanding the Psychiatric Consequences of AIDS," present theoretical position papers. Only a few report on empirical studies (e.g., "Suppression of Human and Mouse Lymphocyte Proliferation by Cocaine"), and the relevance of a few of the chapters to AIDS or HIV is never stated by the authors.

The problems of the book are several and relate to the variable quality of the chapters, the lack of a consistent style, and the absence of a cohesive editorial voice. It is difficult to imagine that any single reader will find more than a few chapters of interest because of the inconsistent and wandering quality of the volume in terms of subject, methods, and purpose. Although the titles of some chapters suggest intriguing subjects, such as "Voodoo Death, the Stress Response and AIDS" and "Gender Differences in Response to HIV Infection," rarely is any new information or original thinking actually provided to the reader.

The first-listed editor of this book, T. Peter Bridge, states that the "chapters in this volume persuasively argue that HIV infection is a neuropsychiatric disorder as well as an immunologic disorder" (p. 9). Most readers who seek out this book will probably not need to be convinced that neuropsychiatric disease can result from HIV infection; however, they may be looking for principles that could link together the many threads constituting this complex new disease process. Although this book touches on some interesting topics at the frontiers of the neurosciences in fields such as psychopharmacology and psychoimmunology and provides some useful summaries, I believe that the editors fail in general to present a volume that will meet the needs of most potential readers. The absence of virtually any clinically oriented material further limits the usefulness of this book for psychiatrists.

This is not the first edited volume to be published on topics related to AIDS and psychiatry, but its title suggests that it may be the most comprehensive and substantive to date. In fact, the book will inform some readers about important topics related to AIDS as a neuropsychiatric disorder, but overall it may serve to disappoint far more readers who expect a thoughtful and coherent editorial approach in a volume that promises to describe such a complicated new field.

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### **HIV and the Nervous System,** *edited by Stanislaw Kubicki, H. Henkes, U. Bienzle, and H.D. Pohle. New York, Gustav Fischer (VCH), 1988, 227 pp., $58.00.*

I remember my first psychiatric consultation involving a young man with AIDS in 1984. We had been called to see this patient because of bizarre behavior and cognitive difficulty. Psychiatric evaluation revealed subacute, fluctuating global impairments in cognition, including disorientation, memory, and attentional difficulties. We accurately diagnosed delirium and headed for the library to look up the CNS complications of AIDS. Our literature review at that time documented only concern about the secondary CNS infections associated with AIDS such as toxoplasmosis or cryptococcus. Only later did we, as well as the scientific community, become aware of the real cause of our patient's CNS symptoms: HIV is a neurotrope that directly attacks the brain and peripheral nervous system, with diffuse impairment in brain structure and function.

*HIV and the Nervous System* is an edited volume of proceedings from the 1987 Berlin Symposium on Neurological Aspects in AIDS. In a series of 34 chapters, the book documents the progress in understanding the neurological aspects of AIDS. The authors focus on neurological rather than psychiatric manifestations of AIDS, with discussions of findings in neuropathology, CSF, EEG, brain imaging, and neuropsychology.

This book covers in detail what we have learned about AIDS and the brain. HIV frequently attacks the brain directly, often early in the course of infection. The CNS involvement produces signs and symptoms, including headache, fatigue, paresthesias, and cognitive impairment. Abnormal EEGs are common in AIDS; abnormalities include slow alpha basal activity, dysrhythmias, and generalized slowing. EEG sleep studies show marked impairment in sleep architecture, with reduced REM time and minimal numbers of sleep spindles. CSF studies frequently reveal nonspecific (pleocytosis, impaired blood-brain barrier) and specific (locally produced anti-HIV antibodies) findings. The CSF findings are frequently found early in the course of AIDS, before CNS signs or symptoms, suggesting early asymptomatic brain infection. Magnetic resonance imaging is superior to CT in demonstrating the structural brain imaging deficits in AIDS, characteristically diffuse and focal leucoencephalopathy.

This book would be particularly useful for psychiatrists in consultation-liaison roles. The chapters are generally well written in a case-series and case-control methodology format. Limited attention is given to psychiatric issues such as depression or adjustment disorder in AIDS, giving this volume less widespread appeal for general adult psychiatrists. As with all books, the volume does not address more recent AIDS and CNS issues, such as the CNS response to treatment with zidovudine (AZT) or other anti-HIV agents. Nevertheless, it provides an excellent review of the brain effects of AIDS and emphasizes the need for neurologists and psychiatrists to become involved in the evaluation and treatment of patients with AIDS.

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### **Surviving and Thriving With AIDS, vol. II:** Collected Wisdom, *edited by Michael Callen. New York, People With AIDS Coalition, 1988, 368 pp., $20.00 (paper).*

Susan Sontag, in her recent book *AIDS and Its Metaphors* (1), states that the metaphors used regarding AIDS suggest that people with the disease have done something wrong and immoral and, as a result, have brought the condition on themselves—a kind of retribution. She believes this can lead to unnecessary hopelessness among patients and panic on the part of the public. Volume two of *Surviving and Thriving With AIDS,* edited by Michael Callen, is meant to dispel myths and to provide those who have AIDS and those who love and care for them with a picture of the reality of the experience, the courage of those with AIDS, and the hope and joy that can still exist for them. The photographs throughout the book, primarily by Jane Rosett, record the human experience that connects us with patients and their loved ones.

In his introduction, Callen states that this book is "the legacy of many who have come before you" and "represents the collective wisdom" of those who are struggling against AIDS. In it we learn about the diverse ways people with AIDS attempt to cope with the illness and lead their lives. Although it is not comprehensive, the writings come from an enormous range of people and are graphic, poignant, and informative. This book is particularly important for those in the mental health disciplines because we can learn about an experience we must share and yet are often unprepared to face.

Physicians who have contributed to the volume describe treatment approaches, including their frustrations and hopes in working with people with AIDS. Families tell us how to share and how to reach out.

The book covers a wide range of topics related to AIDS, including the emotional responses to the diagnosis, AIDS-related complex and having a positive HIV test result, treatments available, survival with AIDS, love and sex and AIDS, family and friends, women and AIDS, people of color and AIDS, AIDS and intravenous drug use, AIDS in prison, children with AIDS, and political responses to AIDS. In addition there is a history of the People With AIDS Coalition self-empowerment movement and a section considering how people who do not have AIDS are involved in the fight against the disease. Finally, the book provides some resource materials, including dealing with disability insurance, Social Security, and Medicaid as well as the organizations that have been helpful to AIDS victims.

Although there are places where disagreement or controversy is apparent, it is essential that we understand the experience of AIDS not only from our own scientific literature but from those who live with it.

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## LONGITUDINAL STUDIES

**Life-Span Research on the Prediction of Psychopathology,** *edited by L. Erlenmeyer-Kimling and Nancy E. Miller. Hillsdale, N.J., Lawrence Erlbaum Associates, 1986, 310 pp., $36.00.*

Dr. Miller begins her introduction to this vast collection of research efforts by dedicating it to "those investigators who are courageous enough, persistent enough, long-lived enough, and some might say misguided enough, to embark on the tantalizing, yet arduous—ever treacherous—search for clues to the origins and development of mental disorder, by virtue of systematically following the unfolding of individual lives over time." This is a fitting introduction to a volume that is impressive in most respects and also somewhat troubling. Dr. Miller accurately describes the struggle of the investigator between "the demands of the methodological rigor and the constraints of the practical research world." A parallel analysis may be made of this volume because the inconsistency of the available knowledge on prediction of psychopathology throughout the life span allows for the brilliance of individual chapters to shine but makes for an incomplete database on the life span. This is less a criticism of any of the chapters and more a comment on the state of knowledge in the field. However, it is heartening that most of the findings presented reflect recently acquired data, indicating the rapid progress that continues to be made in most of the domains of inquiry.

The studies included in this volume survey predictions of psychopathology throughout the entire life span, beginning with prenatal experience and going on to adolescence, the elderly, dementia, and predictors of mortality. Very positive features of this book are several excellent discussion chapters that review what the reader has sifted through and critique each chapter's methodological strengths, empirical reliability, and validity. The discussions written by Gittelman, Robins, Vaillant, and Gruenberg are especially useful in examining the research and focusing clearly on what may have been absent from some of these fine efforts that ought to be considered in future investigations.

In spite of the inherent difficulties in putting together a volume that not only focuses on the challenging task of predicting psychopathology but also attempts to bring together such a wide spectrum of populations and illnesses, much valuable and insightful work is presented here. Cornblatt and Marcuse's research on predictors of schizophrenia in children reveals that sustained attention, distractibility, and short-term memory are all significant variables that may be assessed by trained clinicians working with the offspring of schizophrenic patients. Dr. Tsuang's finding that memory deficit, thought blocking, social withdrawal, auditory or visual hallucinations, and younger age at onset are predictive of a poor outcome in schizophrenic adults is also extremely valuable information for the clinician as well as the researcher. Dr. Weissman et al. present compelling evidence that although depressive symptoms increase the likelihood of a full-blown disorder (thus supporting early therapeutic intervention), the presence of depressive symptoms alone does not significantly raise the risk of mortality. Several other studies presented here not only provide useful information for clinicians and investigators but more generally advance the knowledge base of what should and should not be considered valid predictors of psychopathology over time.

For those conducting or planning further research, Dr. Labouvie's chapter, "Methodological Issues," is extremely valuable. He emphasizes the importance of examining a variety of variables in order to better understand the presence and the prediction of psychopathology. Dr. Labouvie cautions researchers not to focus on a single causal antecedent (as Dr. Miller notes some of the researchers in this volume have done) but, rather, to focus on the principle of multiple causation—that psychopathology emerges from a broad spectrum of pathological, psychosocial, and behavioral events.

Even with the discussion chapters, this book is still more a series of sections than a coherent whole. The overriding value is that there is a plethora of useful investigative work, both for clinicians looking for early signs of psychopathology and for investigators interested in the predictors and course of illness. As such it is best placed on our bookshelves and read one or two chapters at a time rather than attempted in one sitting.

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*Reprints of Book Forum reviews are not available.*

# Letters to the Editor

## $T_3$ Augmentation of a Tricyclic Antidepressant in a Patient Receiving $T_4$ Maintenance Therapy

SIR: While the thyroid hormone triiodothyronine ($T_3$) can apparently potentiate the clinical effects of tricyclic antidepressants (see reference 1 for a review), the usefulness of the related hormone L-thyroxine ($T_4$) for this purpose has been questioned (2, 3). The following case supports the notion that $T_4$ lacks the tricyclic-augmenting properties of $T_3$.

> Ms. A, a 33-year-old woman was referred from another psychiatric inpatient setting for reassessment of refractory depression of 12 months' duration. Upon transfer, a thorough medical workup, including thyroid screening, revealed no abnormalities, and clinical review of the results of a standardized psychiatric diagnostic interview (4) yielded a *DSM-III* diagnosis of major depression. Following unsuccessful trials of numerous antidepressant drug regimens and ECT, the patient eventually exhibited partial improvement after 2–3 weeks of amitriptyline, 200 mg/day, combined with $T_3$, 50 μg/day.
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> Following discharge, Ms. A remained reasonably well for 14 months, at which point recurrent symptoms of fatigue and depressed mood prompted an endocrinologic consultation. Hashimoto's thyroiditis was diagnosed on the basis of a thyroid nodule detected by ultrasound and thyroid antimicrosomal antibodies in serum. $T_4$, 0.15 mg/day, was initiated, and the $T_3$ was discontinued. The patient then noted a further deterioration in her mood, which failed to respond to treatment with tricyclic antidepressants over a period of 3 months.
>
> Readmitted to the hospital in a severely depressed state, Ms. A did not benefit from the tricyclic doxepin in doses up to 300 mg/day prescribed for more than 1 month. $T_3$, 25 μg/day, was then reintroduced, and in order to avoid iatrogenic hyperthyroidism, the $T_4$ was simultaneously reduced to 0.05 mg/day. A dramatic normalization in mood occurred 6 days later. $T_4$ was then discontinued, and the patient remained well 5 months later with continued $T_3$ and doxepin therapy.

While definitive conclusions cannot be drawn from a single case, it is striking that this patient twice experienced an antidepressant response to $T_3$ combined with a tricyclic but exhibited worsening depressive symptoms and failed to respond to tricyclics during treatment with $T_4$. Thyrotropin serum levels were normal before the first course of $T_3$ treatment and were suppressed during $T_4$ therapy, indicating adequate dosing with the latter hormone. Thus, the beneficial effects of $T_3$ in this case cannot be attributed to correction of a subclinical hypothyroidism. These observations support a recent suggestion that $T_3$ is more effective than $T_4$ as an adjunct to tricyclic antidepressants (2).

Since $T_4$ is converted to $T_3$ in the brain (3), the hormones have often been considered interchangeable in the treatment of depression (1, 5). However, Joffe et al. (3) speculated that exogenous $T_3$ may benefit euthyroid depressed patients through suppression of endogenous $T_4$ synthesis, resulting in reduced availability of $T_4$ for conversion to $T_3$ in the brain and lowered brain $T_3$ levels. In contrast, administration of exogenous $T_4$ would increase brain $T_3$ levels. If this model is valid, then it may have been important for this patient that the more recent course of $T_3$ therapy was coupled with a reduced dose of exogenous $T_4$. Studies conducted in depressed patients with concurrent thyroid failure may shed further light on the differential effects of the two thyroid hormones in depression.

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## Single Photon Emission Computed Tomography in Phencyclidine and Related Drug Abuse

SIR: We have recently performed single photon emission computed tomography scans on five consecutive psychiatric patients identified for their illicit phencyclidine (PCP) use. The patients were between the ages of 19 and 26 years. Four were male (three black and one white) and one was female (white). All were using other drugs, including cocaine, alcohol, and marijuana. Although several were intoxicated upon admission to the hospital, all five patients had largely normal findings on physical and neurological examinations. No persistent major cognitive deficits were found in routine clinical testing.

The scans for each subject were performed several days after detoxification (PCP serum or urine concentrations were normal). The ligand used was either iophetamine iodine-123 or HMPAO technetium-99m. Each scan displayed perfusion abnormalities in the cerebral cortex (compared to normal scans obtained by the same techniques). In four of the patients there was asymmetry, with relative decrements in the right hemisphere. Defects varied among frontal, parietal, and temporal regions. One patient appeared to have bilateral abnormalities.

To our knowledge this is the first report of such findings. PCP has long been thought to interfere with cognition, even in low-dose chronic use (1). Another group of researchers has reported scan abnormalities in cocaine users (2). In their report it is unclear whether the subjects had previously used cocaine. The predominance of right-side findings may be consistent with reports of right-left cortical differences in schizophrenia (3). A number of reports have compared PCP users with schizophrenic patients. In this regard, the implication of temporal and frontal lobe deficits in the scan patients is of interest (4).

This is only a preliminary report. The number of subjects was small, and all were multiple drug users. It is therefore unclear what combination of drugs might have accounted for such findings. It is also unclear whether the defects seen on the scans are transient or permanent. Work is now in progress to clarify these issues.

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## Antidepressant and Cognitive Behavior Therapy for an AIDS Patient

SIR: A recent article by Frederick W. Schaerf, M.D., Ph.D., and associates (1) discussed the role of ECT in treating major depression in patients with human immunodeficiency virus (HIV) infection or acquired immune deficiency syndrome (AIDS). Psychological management of depression has often included cognitive behavior therapy (2), which is now a well-established modality. We wish to report on an AIDS patient, admitted to the hospital with a major depressive disorder, who responded to treatment with a combination of antidepressant therapy and cognitive behavior therapy.

Mr. A, a 37-year-old white homosexual male, was diagnosed as HIV positive following pneumocystis carinii pneumonia. He took the diagnosis well; however, 3 months later, after moving into a new apartment, he started to feel sad, low, and miserable. He withdrew from his friends, family, and lover of 4 years' standing. He lost his appetite, slept poorly, had no energy, and had poor concentration. He wished he were dead but did not make any suicidal gestures. He felt hopeless, helpless, and worthless.

In view of his major depressive disorder, Mr. A was admitted to an acute ward. On admission it was noted that his affect was depressed, he had very low self-esteem, and he expressed ideas of self-blame and hopelessness. While on the ward he was started on the antidepressant dothiepin, 150 mg/day p.o. Because of his negative view of himself, the world, and the future, it was decided that he was a suitable candidate for cognitive behavior therapy. Four weeks after admission and the start of antidepressant therapy, he had his first cognitive behavior therapy session. His Beck Depression Inventory score at the first session was 41. The score fluctuated between 40 and 25 over the next eight sessions; by the 12th session it had dropped to 10, where it remained over the next three sessions. The original contract for 10 therapy sessions was extended to another 10 sessions. He was discharged from the hospital after the first three sessions of the second series and received the rest of the treatment as an outpatient.

During these sessions the emphasis was on Mr. A's negative automatic thoughts and on behavioral tasks. At about the 13th session, he was noted to have a tumor in his lung, which was treated as a tubercular lesion. His lover was hospitalized with AIDS-related complex during the same period. Mr. A's dothiepin was reduced to a maintenance dose (75 mg/day). He has not been able to attend the clinic lately, but telephone contact has revealed that he is well mentally and is coping with his physical problems and the additional stress due to his lover's illness.

The application of cognitive behavior therapy to patients with life-threatening illnesses such as cancer is currently receiving clinical and research scrutiny (3). Similar principles have been used with HIV and AIDS patients as well as the worried well (4). Our case illustrates the use of these methods with an inpatient with AIDS and a major depressive disorder. Thus, a therapeutic program that combines physical and cognitive approaches may prove suitable for patients with HIV and AIDS.

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## ECT for a Patient With Profound Mental Retardation

SIR: A profoundly mentally retarded woman with atypical symptoms of major affective disorder was successfully treated with ECT. She had suffered through at least six similar distinct affective episodes, which had lasted as long as 18 months. I could find very few reports in the literature regarding use of ECT in mentally retarded patients (1–3).

Ordinarily, Ms. A was cheerful, cooperative, and alert. She was able to make her wants known, feed herself, and perform some simple self-care. However, she became much less responsive, lost interest in eating, and ignored ward activities. Within 2 months she had become totally disoriented and unresponsive to verbal stimuli. Her screaming and crying alternated with hysterical laughter. She remained awake and agitated all of the time. Her pulse increased to 154 bpm, and her blood pressure became mildly elevated. Her temperature rose above 101 °F. She continually looked over her shoulder in a stereotyped fashion. She showed left facial weakness, clenching of both fists, and a constant purposeless movement of her left hand and arm. Her wrists had to be bound to the sides of the bed to prevent her from pounding herself and others with her fists. She resisted feeding and refused to take fluids. A nasogastric tube was required to prevent dehydration and to correct nutritional deficits.

As in the past, no consistent relief was obtained by use of chlorpromazine, thioridazine, lithium, or trimipramine. A magnetic resonance imaging scan under general anesthesia and a therapeutic trial of prednisone for possible CNS vasculitis were not helpful.

Judicial approval for ECT was sought and granted. Ten treatments were given, at the rate of three times per week, with a Mecta SR 2 instrument set to produce a 0.8-A square wave current with a pulse width of 1.4 msec at a frequency of 70 H and a duration of 1.25 seconds. The average duration of seizure activity was 37 seconds, as measured by single-channel EEG. General anesthesia was produced with atropine, 0.6 mg; methohexital, 80 mg; and succinylcholine, 70 mg.

Ms. A showed a dramatic response by the sixth treatment, and all of the active signs of the disease process were resolved by the time the ECT series was completed. The patient remained weak and uncoordinated but was alert, cheerful, eating, and generally her old self again. Her blood pressure and pulse returned to normal. Her left fist relaxed, the left facial droop disappeared, and she stopped looking over her shoulder. Restraints were no longer required. She took an interest in her surroundings.

This mentally retarded patient was restored to health, with minimal risk and side effects, by ECT.

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## Reappearance of Menses in a Patient Taking Fluoxetine

SIR: A 50-year-old woman with a 20-year history of severe obsessive-compulsive disorder, whose condition had been stabilized on a regimen of 300 mg/day of doxepin and 32 mg/day of perphenazine, was able to reduce these medications to 100 mg/day of doxepin only after fluoxetine, 20 mg/day, was added. Her symptoms were alleviated and she was able to seek employment. Five months after the changeover, her menses reappeared at regular monthly intervals (they had stopped 2 years earlier). One gynecologist felt that this renewed bleeding must be pathological. I sent her to an endocrinologist who is familiar with psychiatric medication, and he agreed that her menses had been suppressed by the doxepin and perphenazine and then had escaped this suppression when she took fluoxetine. The advice of the gynecologist prevailed, and a dilatation and curettage was done, which revealed no abnormalities. A second gynecological consultant to whom I sent the patient reviewed the slides and felt that the patient had not been menopausal in the first place. Six months later, continuing to take fluoxetine, 20 mg/day, the patient resumed taking a lower amount of perphenazine (8 mg/day) and her menses again ceased, only to reappear when she stopped the perphenazine 2 months after that.

I present this case, at a time when many patients' medication is being changed to fluoxetine, in the hope of preventing unnecessary curettage and even hysterectomy based on the mistaken assumption that the reappearance of menses while a patient is taking fluoxetine is pathological.

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## A Case of Malingering

SIR: We would like to report an unusual case of malingering.

> Mr. A, a young soldier without prior psychiatric history, worked at an isolated Pacific post that stockpiles neurotoxic agents. He complained one morning of photophobia. His local physician noted a fixed dilated right pupil and sent the patient to our hospital for evaluation. A neurologist and ophthalmologist considered pharmacologic blockade to be the likely cause of his symptom. Adie's pupil was considered, but the absence of a response to pilocarpine made this diagnosis unlikely (1). Mr. A was returned to duty, but 2 weeks of persistent symptoms led to his return to our hospital. Two neuro-ophthalmologists examined him and considered pharmacologic blockade likely, but they were uncertain about the etiology of the dilated pupil. A CT scan of the head and orbits was unremarkable.
>
> Mr. A was seen by a psychiatrist in consultation and was admitted to the hospital for evaluation. A search of his belongings yielded nothing unusual. The patient's only concern was to discover the cause of his visual problem. He seemed nonchalant and wore an eye patch on the ward. Although his isolated duty separated him from his wife and child for periods of 5 months, he denied any psychiatric symptoms. His mental status evaluation was unremarkable except for his insouciance. He denied taking drugs. There was no history to suggest antisocial personality disorder or factitious disorder.
>
> After 2 weeks of uneventful observation of Mr. A, a property search was conducted on the ward because a visitor was suspected of distributing illicit drugs. When Mr. A's belongings were searched, an altered deodorant stick was noted. Inside the container was a small unlabeled bottle. At this point the patient excitedly revealed that the bottle contained atropine. He confessed that he used the drops to dilate his pupil so that he could escape duty at his isolated post.

This patient's symptom obscured his goal of avoiding duty but, clearly, avoiding duty was the goal. This external incentive indicated that the diagnosis should be malingering rather than factitious disorder. Malingering is not considered a mental disorder but must be considered in psychiatric diagnoses (2). Neurologists and ophthalmologists are aware of this possibility (3), but there is little note of malingering in the psychiatric literature. The evaluation of the patient emphasizes the importance of making a diagnosis on the basis of direct evidence rather than making a diagnosis by ruling out other possible diagnoses.

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## An Etiological Factor in Drug Addiction

SIR: When I went to medical school, I was taught that more mistakes are made by not looking than by not knowing.

A distinguished biochemist, Roger Williams (discoverer of pantothenic acid), did an interesting controlled experiment (1). A group of rats was given a junk food diet and a free choice of water or dilute alcohol to drink. The rats chose the alcohol and left the water alone. A control group of rats was given an optimum diet and the same choice of liquids. The control group took the water and left the alcohol alone. Obviously, rats are not people, but the principle seen in the rat experiment appears to be applicable to humans, in view of the large number of people eating junk food and the large number of drug addicts. Alcohol is an addictive drug that has many similarities to other addictive drugs.

I wonder if the people who are fighting President Bush's war against drugs are not looking widely enough.

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## Child Sexual Abuse in West China

SIR: Because of the increasing number of reports in the North American literature on adult patients with a variety of psychiatric disorders who have histories of childhood sexual abuse, I thought that *Journal* readers might be interested in the experience of a Chinese clinician in the People's Republic of China.

During the past 3 years I have seen 27 women (out of a total of 158 women patients) with histories of sexual experiences during childhood. These 27 patients were between the ages of 16 and 38 years when they first consulted me. Eighteen were the victims before the age of 13 of rape or sexual molestation involving genital contact by males who were 16 or more years old. Nine patients had engaged in sexual intercourse without coercion before the age of 14, in some instances with childhood male playmates. Twenty-five of these patients suffered from a variety of anxiety disorders according to *DSM-III-R* criteria: 21 had generalized anxiety disorder, three had obsessive-compulsive disorder, and one had simple phobic disorder. Of these 25 individuals, 12 also had depressive disorders (three had major depression, seven had dysthymic disorder, and two had atypical bipolar disorder). Of the remaining two women with histories of childhood sexual experiences, one was diagnosed as having functional dyspareunia and one as having functional nocturia.

Ten of the patients were married and 17 were single. Twelve were students, nine were blue-collar workers, four had administrative jobs, and two were teachers. Only two of the 18 patients who had been raped or sexually molested had reported the offense to the authorities, fearing retribution by the offenders, punishment by their parents, or a variety of social penalties, such as a loss of the opportunity to complete their education.

Treatment, which lasted more than a year for only nine patients, consisted of counseling and psychotherapy, combined with pharmacotherapy when indicated. All of the patients achieved some degree of relief of symptoms and social distress, although the lack of formal quantitative measurements does not permit a more specific categorization of the extent of their improvement.

Any generalizations from these data must be made with caution. The figures were derived from a retrospective analysis of my clinical records and do not necessarily reflect the true incidence of childhood sexual activity and abuse in my own patients or in the population at large. Furthermore, the information about the patients' social backgrounds, their reactions to their experiences, and the results of treatment is unavoidably impressionistic, since it is based on clinical notes made in the course of the busy practice of a clinician who was not specifically concerned with investigating child abuse at the time he saw these patients. To be fully reliable, such information must, of course, flow from a systematic prospective study of the phenomena under investigation. At the same time, it is not without interest that despite these methodological failings, a number of my patients presented histories of childhood sexual abuse. One may conclude that such abuse is not restricted to selected regions and cultures on our earth, but that it is a universal, cross-cultural clinical problem and, as such, warrants study by psychiatrists, whatever their national and cultural boundaries.

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## Dosage of Fluphenazine

SIR: I read with interest the article by Lawrence B. Inderbitzin, M.D., and associates concerning the problem of dosage of fluphenazine decanoate (1). It is a strange fact indeed that dosage of neuroleptics in clinical practice varies within an extremely wide range and that the question of determining the appropriate dose for the individual patient is still to be resolved. I would like to add two comments, one critical and one affirmative.

First, it seems a bit arbitrary to convert fluphenazine decanoate to oral fluphenazine at a ratio of 12.5 mg/3 weeks to 10 mg. The authors should at least have mentioned the diversity of opinion in the literature about this conversion factor; some investigators have stated that they were unable to find a reliable conversion factor at all (comparing plasma levels) (2). Furthermore, the conversion factor chosen by Dr. Inderbitzin and associates seems to favor the parenteral application, which requires very high oral doses, thus fostering the article's hypothesis that dosing of fluphenazine decanoate is too high. In Austria the manufacturer's recommendation for conversion is 25 mg/3 weeks of fluphenazine decanoate for 10 mg of the oral drug, and some authors recommend an even lower proportion of oral fluphenazine (manuscript of L. Ereshefsky et al., University of Texas, 1984).

Considering that the difference between oral and parenteral dosage might not be as big as reported owing to these considerations, the crucial point still remains: application of fluphenazine as a depot drug leads to higher dosage. A colleague and I came to similar conclusions in comparing the intravenous application of fluphenazine to the oral application as routinely administered in two Austrian state hospitals (H. Rittmannsberger and H. Unterluggauer, manuscript to be published). During the first week of treatment, patients receiving intravenous fluphenazine (drips) received an average of 51 mg/day, whereas the dose of the group treated with oral fluphenazine averaged 35.7 mg. The high loss of active drug due to the first-pass effect makes the difference between the two forms of application still greater. Nevertheless, clinical outcome in the two groups of patients was about equally good, as rated with the Brief Psychiatric Rating Scale (BPRS). The only significant difference in BPRS scores was on anergia, where the group taking oral medication did better. So one of the conclusions of our study was that the usually administered doses of intravenous fluphenazine are higher than necessary.

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Sir: As we currently are involved in a large multicenter study concerning the use of depot neuroleptics, we are prompted to comment on the article by Dr. Inderbitzin and co-workers, which we read with interest but also with some bewilderment. We want to emphasize the following points.

In our opinion the method described by the authors raised the following unclarified issues. 1) It is not clear whether all patients selected for their study were outpatients. 2) Whereas the patients receiving the depot drug were randomly selected from a pool of *about* 100 patients (the results give the impression that there were exactly 90 patients receiving fluphenazine decanoate), nothing is said about the pool from which the patients receiving the oral medication were drawn. 3) We hope that the interrater reliability was excellent for the sociodemographic variables such as sex, age, and race; or do these data concern the raters themselves? 4) On which data was the conversion factor of 12.5 mg/3 weeks equals 10 mg of oral fluphenazine based? In the literature a number of such conversion factors are given, varying by at least a factor of 5! 5) Did the authors mean a daily dose of 10 mg of oral fluphenazine? The formula presented can be interpreted in such way that the dose (given as chlorpromazine equivalents) is calculated as dose per week. 6) Calculating the results to a standard interval of 3 weeks is not allowed, as was shown by Hargreaves et al. (1). 7) According to information obtained from the supplier of fluphenazine, the tablets contain 86% pure fluphenazine, whereas the decanoate form contains 74% pure fluphenazine.

Given these comments, it is difficult or impossible to interpret the results of the study, as may be shown by the following. 1) It is not clear whether the mean chlorpromazine equivalent dose (2010±836 per what?) was higher than the 373±384 (per day?) oral dose. 2) Recalculation of the data given in table 1 results in a mean dose of 1997±838 mg, which is different from the outcome given by the authors. We presume that, according to a statement by the authors, oral medication was not included in the calculations. 3) Saying that 1404 mg/day (the value obtained for 90 patients) is *somewhat* lower than the 2010 mg/day calculated for 20 patients is apparently not based on statistics.

Of course, we agree with the authors that too little is known about how depot neuroleptics are prescribed in daily practice, but to us it does not seem justified to say that "the use of fluphenazine decanoate may come at the inadvertent cost of a significantly higher dose for a subgroup of patients." Furthermore, it seems very important not only to compare the amount of depot neuroleptic medication patients are taking but to include their other medications as well.

In conclusion, we would like to state that we disagree with the article. However, we hope that at least this article, together with our letter, will start a discussion about the use and knowledge of depot neuroleptics.

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## Drs. Inderbitzin and Lewine Reply

Sir: As stated in our previously published letter (1), we agree that there are no definitive data on which to base a secure conversion factor and that other authors have suggested other equivalencies. As stated by Yadalam and Simpson (2), "Most published schedules [conversion formulas] will result in excessive doses of fluphenazine decanoate for many patients."

The analysis of our data was based on the assumption that 25 mg of fluphenazine decanoate every 3 weeks equals 1000 mg/day of chlorpromazine. We have subsequently reanalyzed our data using a much lower (one-half the earlier) equivalency (25 mg/3 weeks equals 500 mg/day of chlorpromazine), as suggested by a recent review of $ED_{50}$ studies (3). The differences between the mean doses of our two groups (oral fluphenazine versus fluphenazine decanoate) were still significant at the 0.001 level. If the oral medications that were also being taken by the decanoate group had been included in the calculations, the reported differences would have been even greater. Furthermore, noncompliance among patients in the oral group could have decreased the actual mean dose taken by that group by as much as 50% (4).

It is clear to us that *no one* knows exactly what numbers to use, and decisions about depot neuroleptic therapy remain clinical and empirical. We are gratified that Dr. Rittmannsberger and associates have studied this issue empirically and concluded, in agreement with our study, that "the crucial point still remains: application of fluphenazine as a depot drug leads to higher dosage."

Prudent clinicians will seek doses that are appropriately effective and safe, and these are likely to be lower than those used in the past.

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## Antidepressants in the Treatment of PTSD

SIR: We read with interest the recent report by Christopher Reist, M.D., and associates on the use of desipramine in the treatment of posttraumatic stress disorder (PTSD) (1). Their finding that desipramine was significantly effective for depressive symptoms but ineffective for specific symptoms of PTSD is at variance with our own recent work. In our study (2), symptoms of PTSD, but not depression, improved significantly after treatment with imipramine or phenelzine, compared to placebo, during an 8-week trial.

Several factors may account for this discrepancy. Dr. Reist and associates studied inpatients with PTSD. One-third of these patients also had major depression, and an unspecified number were current alcohol abusers who had been abstinent for a minimum of 2 weeks. By contrast, our subjects were outpatients, many with minor depression but none with a full-blown depressive syndrome. We also required a minimum of 4 weeks' abstinence from alcohol before treatment. The lack of agreement between the findings of Dr. Reist and associates and our findings may reflect both real differences in the drug responses of these diagnostically different samples and methodological differences between the two studies.

While we do not disagree that antidepressants may ameliorate the depressive symptoms in patients with PTSD who are also depressed, we suggest that the second conclusion of the desipramine study—that the specific symptoms of PTSD do not improve with antidepressant treatment—may represent a type II error (an inappropriate conclusion of no treatment effect), in this case because of inadequate sample size. Indeed, the nonsignificant trend in the data of Dr. Reist and colleagues toward showing a drug effect on intrusive PTSD symptoms suggests that a larger study might have yielded significant results. We also question whether their dosing strategy was adequate, since they verified blood levels only after the trial was completed and some subjects were out of the therapeutic range. Finally, a 4-week trial may be insufficient to find subtle drug effects, since recent work suggests that not all symptoms respond to antidepressants at the same rate. Some symptoms do not improve until week 5 or 6 (3). Indeed, a forthcoming report of a study comparing amitriptyline to placebo in patients with PTSD concludes that in this condition some drug effects do not appear before week 8 (4).

In sum, despite the countervailing report of Dr. Reist and associates, we believe our 8-week trial of 34 subjects with documented therapeutic blood levels of medication constituted a stronger test of the hypothesis that antidepressants may benefit specific PTSD symptoms, such as nightmares, flashbacks, and intrusive recollections, separate from their effects on depression. In light of the sample and methodological differences between the studies, which we have discussed, the findings of Dr. Reist and associates should be interpreted with caution.

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## Concept of Interpersonal Distance in Borderline Personality Disorder

SIR: Frederick T. Melges, M.D., and Marvin S. Swartz, M.D. (1) portrayed borderline patients as displaying a tendency toward alternating interpersonal closeness and withdrawal. I agree with their observation. I also find their explanation for such oscillations to be quite true in my clinical experience. Borderline individuals do fear fusion in closeness and withdraw only to experience abandonment and aloneness. The authors correctly identify the inability to maintain optimal distance in relationships as a central problem in borderline psychopathology.

What troubles me, however, is that Drs. Melges and Swartz overlooked many important earlier references to this very phenomenon. For instance, writing about the schizoid individual, Fisher (2) stated that upon "becoming interested in others . . . he becomes too interested. He suddenly finds himself bound by the strength and tenacity of his own feelings. Then, in an effort to break the suffocating bondage imposed by his incapacitating affective tensions, he unwittingly resorts to emotional withdrawal" (p. 365). Similarly, Guntrip (3), in his description of the schizoid individual, pointed out that "when separated he feels utterly insecure and lost but when reunited he feels swallowed, absorbed, and loses his separate individuality by regression to infantile dependence. Thus he must always be rushing into a relationship for security and at once breaking out again for freedom and independence" (p. 36).

Fisher and Guntrip are of course not the only ones to have described this state of affairs. Balint's (4) concepts of "ocnophilic" and "philobatic" object choices and Burnham et al.'s (5) "need-fear dilemma" are further evidence that earlier investigators clearly recognized the oscillations between closeness and distance shown by those with severe personality disorders. The omission by Drs. Melges and Swartz of these four references, among others, from their survey of the literature is disconcerting.

In all fairness to Drs. Melges and Swartz, I recognize that these references might have been missed because the specific term "borderline" was not used in them. Nonetheless, I believe that since the term "borderline" is relatively new and since there is dubious nosological congruity between the relevant psychoanalytic and descriptive literatures, a more inclusive literature search would have been more productive in the search for important concepts in this area.

More significantly, Dr. Melges and Swartz do not seem to be aware that the term "optimal distance," in this context, was coined in 1958 by Bouvet (6). They also gave short shrift to Margaret Mahler and did not even mention her by name in their paper. Her pioneering work on separation-individuation, especially the conflicts of the rapprochement subphase, has at its very heart the issue of the struggle between fusion and autonomy and, hence, optimal interpersonal (and intrapsychic) distance. To include Mahler among "many psychoanalytic writers [who] have highlighted the patient's problems with separation-individuation" (p. 1118), as the authors did, is akin to saying that Freud is among many analysts who have discussed the mechanism of repression!

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SALMAN AKHTAR, M.D.
*Philadelphia, Pa.*

## Dr. Swartz Replies

SIR: I appreciate Dr. Akhtar's comments, although I find them complementary, not disconcerting. The additional references he cites are worth incorporating in future work. Our literature review was necessarily brief. We intended to maintain an interpersonal focus while presenting a potentially useful clinical heuristic. As a result, a fuller discussion of the relevant psychoanalytic literature was not possible; no short shrift was intended.

Dr. Akhtar's comments raise the issue of specificity in our formulations. Several colleagues have suggested that marked oscillations in attachment, as described, are common to a number of severe personality disorders. This is an interesting empirical issue that goes to the heart of the dimensional versus categorical nosology debate regarding axis II. Borderline personality disorder may be better conceptualized as a dimensional construct. Our paper referred to patients who meet criteria for the borderline diagnosis; a broader view of borderline phenomena should incorporate Dr. Akhtar's remarks.

MARVIN SWARTZ, M.D.
*Durham, N.C.*

## Need for Clearer Thinking About Diagnostic Criteria

SIR: I am writing to address a matter of language and its impact on thinking in our profession. In the August 1989 issue of the *American Journal of Psychiatry*, the lead article (1) addressed the descriptions of the psychotic disorders in *DSM-III-R*. The authors gave a detailed account of the discussions and complex issues that were involved in revising the diagnostic categories and criteria in that section, revealing how the many points of view had to be reconciled and how decisions and choices were made. It was made clear that the categories and criteria that were chosen are in flux and may be revised in the future. This sort of "behind the scenes" material emphasizes the necessity for precisely established criteria and descriptions in psychiatric diagnosis.

However, in the very next article in that issue (2), which was about certain features of bulimia and anorexia nervosa, the language reflects the way these diagnostic criteria often come to be viewed and used. In the first paragraphs, the authors stated, "According to *DSM-III-R*, anorexia nervosa is characterized by . . . ." and, similarly, "Bulimia nervosa, according to *DSM-III-R*, involves . . . ." The use of "according to" and "is" (rather than "is defined as" or some such phrasing) reflects a state of mind in which the categories and criteria of *DSM-III-R* have become reified and codified. "According to" felicitously would be followed by "Holy Writ," and "is" implies being rather than definition and consensus of language. Bulimia is not the same as the criteria for that diagnosis, and the same is true for anorexia nervosa; the criteria are collections of symptoms and observations about patients that have been defined into categories. Giving bulimia and the other diagnostic categories delineated in *DSM-III-R* the status of illnesses is imprecise language and reflects unclear thinking. Pneumococcal pneumonia will not be defined into or out of existence in a few years; bulimia and anorexia nervosa may be redefined and recategorized.

In the teaching I have done with psychiatric residents and in interactions with laypersons (such as attorneys), this mind-set is frequently encountered and has to be corrected. In a "Cautionary Statement" at the beginning of *DSM-III-R* (p. xxix), the editors state, "The specified diagnostic criteria . . . are offered as guidelines for making diagnoses, since it has been demonstrated that the use of such criteria enhances agreement among clinicians and investigators. . . . These diagnostic criteria . . . reflect a consensus of current formulations of evolving knowledge in our field. . . . " I am sure that Dr. Fava and associates are aware of this caution; they started by referring to bulimia and anorexia as "syndromes." As a teacher, I expect to have to remind trainees of these distinctions, and as a psychiatrist, to have to remind other professionals. I would expect, however, that articles in our professional journals would not be written in a way that promotes the sort of thinking in which diagnostic criteria are mistaken for things. How we speak about things (and write about them) both reveals and influences how we think, and it is important to keep our thinking clear.

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MARIAM COHEN, M.D.
*Scottsdale, Ariz.*

## Correction

In the review by Ira D. Glick, M.D., of the book *The Creative Process of Psychotherapy* (May 1989 issue, p. 675), the book's author was incorrectly identified as Arnold Rothenberg. The author of the book is Albert Rothenberg. The book was published in 1988, not 1987.

*Reprints of letters to the Editor are not available.*

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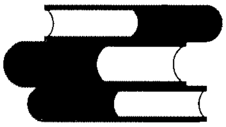

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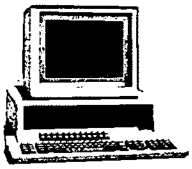

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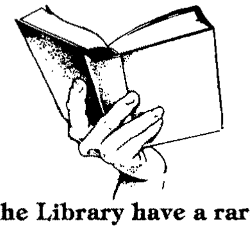

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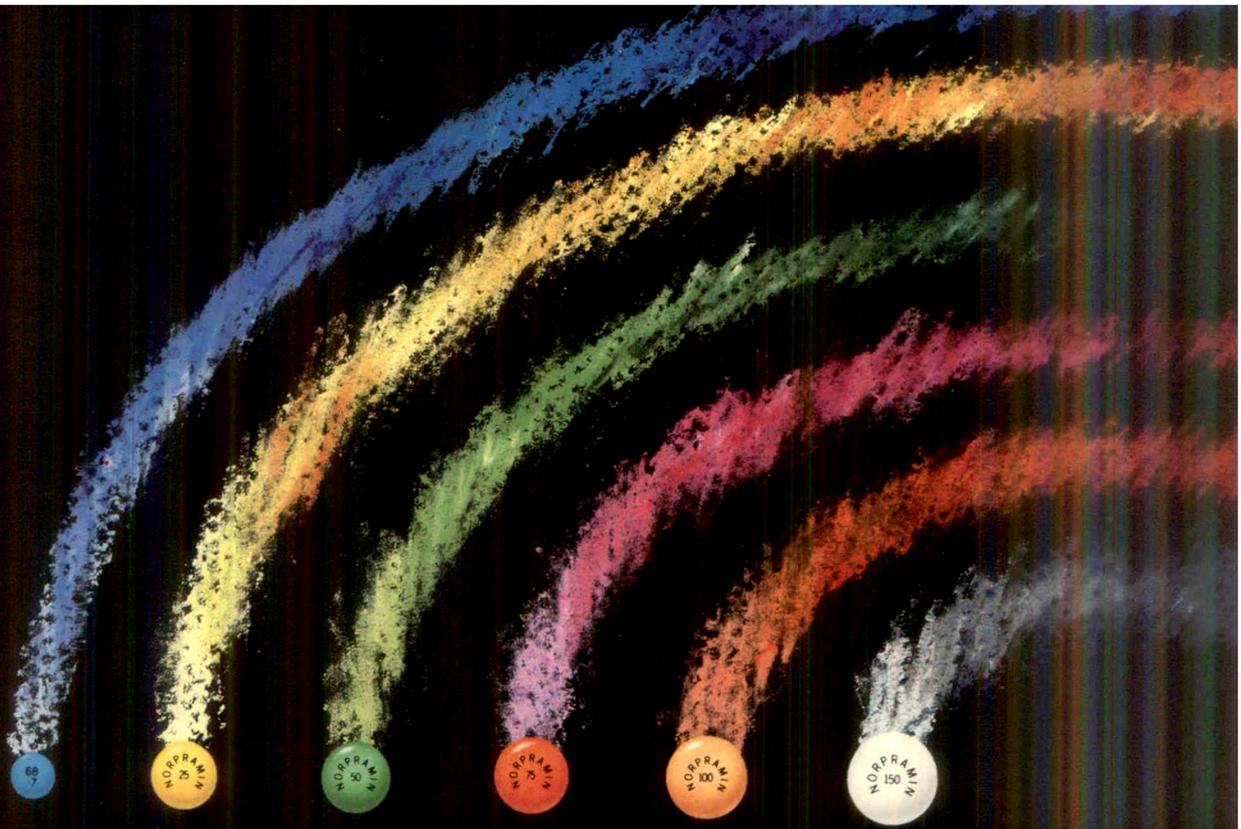

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### CLINICAL PHARMACOLOGY

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The rate of metabolism of tricyclic antidepressants varies widely from individual to individual, chiefly on a genetically determined basis. In general, the elderly metabolize tricyclic antidepressants more slowly than do younger adults.

Certain drugs, particularly the psychostimulants and the phenothiazines, increase plasma levels of concomitantly administered tricyclic antidepressants through competition for the same metabolic enzyme systems. Other substances, particularly barbiturates and alcohol, induce liver enzyme activity and thereby reduce tricyclic antidepressant plasma levels. Similar effects have been reported with tobacco smoke.

Additional information on metabolism appears in Full Prescribing Information.

### CONTRAINDICATIONS

Desipramine hydrochloride should not be given in conjunction with, or within 2 weeks of, treatment with an MAO inhibitor drug; hyperpyretic crises, severe convulsions, and death have occurred in patients taking MAO inhibitors and tricyclic antidepressants. When Norpramin (desipramine hydrochloride) is substituted for an MAO inhibitor, at least 2 weeks should elapse between treatments. Norpramin should then be started cautiously and should be increased gradually.

The drug is contraindicated in the acute recovery period following myocardial infarction. It should not be used in those who have shown prior hypersensitivity to the drug. Cross sensitivity between this and other dibenzazepines is a possibility.

### WARNINGS

1. Extreme caution should be used when this drug is given in the following situations:
   a. In patients with cardiovascular disease, because of the possibility of conduction defects, arrhythmias, tachycardias, strokes, and acute myocardial infarction.
   b. In patients with a history of urinary retention or glaucoma, because of the anticholinergic properties of the drug.
   c. In patients with thyroid disease or those taking thyroid medication, because of the possibility of cardiovascular toxicity, including arrhythmias.
   d. In patients with a history of seizure disorder, because this drug has been shown to lower the seizure threshold.
2. This drug is capable of blocking the antihypertensive effect of guanethidine and similarly acting compounds.
3. **USE IN PREGNANCY**
   Safe use of desipramine hydrochloride during pregnancy and lactation has not been established; therefore, if it is to be given to pregnant patients, nursing mothers, or women of childbearing potential, the possible benefits must be weighed against the possible hazards to mother and child. Animal reproductive studies have been inconclusive.
4. **USE IN CHILDREN**
   Norpramin (desipramine hydrochloride) is not recommended for use in children since safety and effectiveness in the pediatric age group have not been established. (See ADVERSE REACTIONS, Cardiovascular.)
5. The patient should be cautioned that this drug may impair the mental and/or physical abilities required for the performance of potentially hazardous tasks such as driving a car or operating machinery.
6. In patients who may use alcohol excessively, it should be borne in mind that the potentiation may increase the danger inherent in any suicide attempt or overdosage.

### PRECAUTIONS

1. It is important that this drug be dispensed in the least possible quantities to depressed outpatients, since suicide has been accomplished with this class of drug. Ordinary prudence requires that children not have access to this drug or to potent drugs of any kind; if possible, this drug should be dispensed in containers with child-resistant safety closures. Storage of this drug in the home must be supervised responsibly.
2. If serious adverse effects occur, dosage should be reduced or treatment should be altered.
3. Norpramin (desipramine hydrochloride) therapy in patients with manic-depressive illness may induce a hypomanic state after the depressive phase terminates.
4. The drug may cause exacerbation of psychosis in schizophrenic patients.
5. Close supervision and careful adjustment of dosage are required when this drug is given concomitantly with anticholinergic or sympathomimetic drugs.
6. Patients should be warned that while taking this drug their response to alcoholic beverages may be exaggerated.
7. Clinical experience in the concurrent administration of ECT and antidepressant drugs is limited. Thus, if such treatment is essential, the possibility of increased risk relative to benefits should be considered.
8. If Norpramin (desipramine hydrochloride) is to be combined with other psychotropic agents such as tranquilizers or sedative/hypnotics, careful consideration should be given to the pharmacology of the agents employed since the sedative effects of Norpramin and benzodiazepines (e.g., chlordiazepoxide or diazepam) are additive. Both the sedative and anticholinergic effects of the major tranquilizers are also additive to those of Norpramin.
9. Concurrent administration of cimetidine and tricyclic antidepressants can produce clinically significant increases in the plasma levels of the tricyclic antidepressants. Conversely, decreases in plasma levels of the tricyclic antidepressants have been reported upon discontinuation of cimetidine which may result in the loss of the therapeutic efficacy of the tricyclic antidepressant.
10. This drug should be discontinued as soon as possible prior to elective surgery because of the possible cardiovascular effects. Hypertensive episodes have been observed during surgery in patients taking desipramine hydrochloride.
11. Both elevation and lowering of blood sugar levels have been reported.
12. Leukocyte and differential counts should be performed in any patient who develops fever and sore throat during therapy; the drug should be discontinued if there is evidence of pathologic neutrophil depression.

### ADVERSE REACTIONS

Note: Included in the following listing are a few adverse reactions that have not been reported with this specific drug. However, the pharmacologic similarities among the tricyclic antidepressant drugs require that each of the reactions be considered when Norpramin (desipramine hydrochloride) is given.

*Cardiovascular:* hypotension, hypertension, tachycardia, palpitation, arrhythmias, heart block, myocardial infarction, stroke. There has been a report of an "acute collapse" and "sudden death" in an eight-year old (18 kg) male, treated for two years for hyperacti (See WARNINGS, Use in Children.)

*Psychiatric:* confusional states (especially in the elderly) with hallucinations, disorie tion, delusions; anxiety, restlessness, agitation; insomnia and nightmares; hypoma exacerbation of psychosis.

*Neurologic:* numbness, tingling, paresthesias of extremities; incoordination, at tremors; peripheral neuropathy; extrapyramidal symptoms; seizures; alteration in patterns; tinnitus.

*Anticholinergic:* dry mouth, and rarely associated sublingual adenitis; blurred vi disturbance of accommodation, mydriasis, increased intraocular pressure; constipa paralytic ileus; urinary retention, delayed micturition, dilatation of urinary tract.

*Allergic:* skin rash, petechiae, urticaria, itching, photosensitization (avoid exces exposure to sunlight), edema (of face and tongue or general), drug fever, cross sensit with other tricyclic drugs.

*Hematologic:* bone marrow depressions including agranulocytosis, eosinophilia, pur thrombocytopenia.

*Gastrointestinal:* anorexia, nausea and vomiting, epigastric distress, peculiar t abdominal cramps, diarrhea, stomatitis, black tongue.

*Endocrine:* gynecomastia in the male, breast enlargement and galactorrhea in the fem increased or decreased libido, impotence, painful ejaculation, testicular swel elevation or depression of blood sugar levels; syndrome of inappropriate antidiu hormone secretion (SIADH).

*Other:* jaundice (simulating obstructive), altered liver function; weight gain or perspiration, flushing; urinary frequency, nocturia; parotid swelling; drowsiness, dizzin weakness and fatigue, headache; alopecia.

*Withdrawal Symptoms:* Though not indicative of addiction, abrupt cessation of treat after prolonged therapy may produce nausea, headache, and malaise.

### OVERDOSAGE

There is no specific antidote for desipramine, nor are there specific phenomen diagnostic value characterizing poisoning by the drug.

Within an hour of ingestion the patient may become agitated or stuporous and comatose. Hypotension, shock, and renal shutdown may ensue. Grand mal seizures, early and late after ingestion, have been reported. Hyperactive reflexes, hyperpyre muscle rigidity, vomiting, and ECG evidence of impaired conduction may occur. Ser disturbances of cardiac rate, rhythm, and output can occur. The precepts of early evacua of the ingested material and subsequent support of respiration (airway and movem circulation, and renal output apply.

The principles of management of coma and shock by means of the mechanical respir cardiac pacemaker, monitoring of central venous pressure, and regulation of fluid and a base balance are well known in most medical centers and are not further discussed h

Because CNS involvement, respiratory depression, and cardiac arrhythmia can o suddenly, hospitalization and close observation are generally advisable, even when amount ingested is thought to be small or the initial degree of intoxication appears slig moderate. Most patients with ECG abnormalities should have continuous cardiac monito for at least 72 hours and be closely observed until well after cardiac status has returne normal; relapses may occur after apparent recovery.

The slow intravenous administration of physostigmine salicylate has been reporte reverse most of the anticholinergic cardiovascular and CNS effects of overdose tricyclic antidepressants. In adults, 1 to 3 mg has been reported to be effective. In child the dose should be started with 0.5 mg and repeated at 5-minute intervals to determine minimum effective dose; no more than 2 mg should be given. Because of the short dura of action of physostigmine, the effective dose should be repeated at 30-minute to minute intervals, as necessary. Rapid injection should be avoided to reduce the possib of physostigmine-induced convulsions.

Other possible therapeutic considerations include:

(a) Dialysis: Desipramine is found in low concentration in the serum, even aft massive oral dose. In vitro experiments in which blood bank blood was used indi that it is very poorly dialyzed. Because of indications that the drug is secrete gastric juice, constant gastric lavage has been suggested.

(b) Pharmacologic treatment of shock: Since desipramine potentiates the actio such vasopressor agents as levarterenol and metaraminol, they should be used with caution.

(c) Pharmacologic control of seizures: Intravenous barbiturates are the treatmer choice for the control of grand mal seizures. One may, alternatively, consider parenteral use of diphenylhydantoin, which has less central depressant effect also has an effect on heart rhythm that has not yet been fully defined.

(d) Pharmacologic control of cardiac function: Severe disturbances of cardiac rhythm, and output are probably the initiating events in shock. Intravascular vol must be maintained by i.v. fluids. Digitalization should be carried out early in of the fact that a positive inotropic effect can be achieved without increas cardiac work. Many of the cardiodynamic effects of digitalis are the exact oppo of those of massive doses of desipramine (animal studies).

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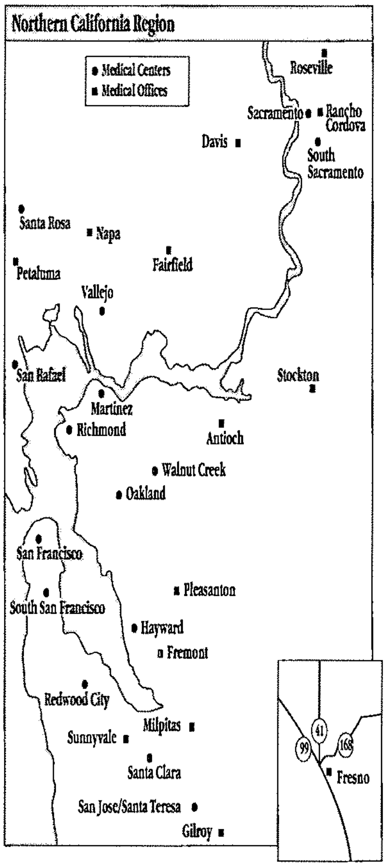

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- Redwood City
- Fresno
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TPMG offers many benefits: scheduled time off with cross-coverage provided by your colleagues, continuing education, malpractice insurance, a substantial retirement program and special arrangements for physicians transferring from established practice. For complete information, call or send CV to: The Permanente Medical Group, Inc., Richmond Prescott, M.D., Physician Recruitment Services, Dept. AJP-7175, 1814 Franklin, 4th Floor, Oakland, CA 94612. (800) 777-4912. EOE

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## PSYCHIATRISTS

BC/BE physicians wanted for full-time positions in our Department of Psychiatry in Stockton, California.

Stockton is an attractive community with its own recreational and cultural attractions and is well located within two hours of the mountains, the ocean and the San Francisco area.

Our group provides a professionally satisfying practice while allowing the time for developing a rewarding personal life.

Salary and benefits are excellent including paid vacation and educational leave, extensive retirement benefits, medical and dental insurance, malpractice insurance and malpractice tail coverage.

*CONTACT:*

*Frederic D. Baker, M.D.*
*Physician-in-Charge*
*The Permanente Medical Group, Inc.*
*1305 Tommydon Street*
*Stockton, CA 95210*
*209-476-3013*

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## CHAIR OF NEUROPSYCHIATRY/ BEHAVIORAL SCIENCE

The University of South Carolina School of Medicine invites nominations and applications for the combined position of Chairman of the Department of Neuropsychiatry and Behavioral Science and Director of the William S. Hall Psychiatric Institute of the South Carolina Department of Mental Health.

Unique opportunity to expand and further develop well-established academic department and state-funded psychiatric institute into combined neuropsychiatric training and research center. Candidates must be board-certified in psychiatry and should have strong administrative and leadership qualities with superior teaching and research credentials.

Applications with curriculum vitae and nominations may be submitted for confidential review by the Search Committee to:

C. Warren Derrick, Jr., M.D.
Chairman of Neuropsychiatry Search Committee
Department of Pediatrics
University of South Carolina School of Medicine
Suite 501
Two Medical Park
Columbia, SC 29203.

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UNIVERSITY OF SOUTH CAROLINA

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# Director of Psychiatry

The Jewish Home and Hospital for Aged, a teaching nursing home and long term care associate of the Mount Sinai School of Medicine, seeks a full-time Director of its Psychiatry Program which spans a spectrum of health care responsibilities.

The position includes responsibility for JHHA's renowned psychiatry program, developing new clinical approaches, teaching medical students, fellows, primary care physicians, and colleagues in other disciplines, research on normal aging, including functional and organic diseases of late life.

Academic appointment and salary commensurate with credentials. Please contact **Leslie S. Libow, M.D., Greenwall Professor, 120 West 106th Street, NYC,10025; Telephone: (212) 870-4866.**

The Jewish
Home &
Hospital
For Aged

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The Department of Psychiatry at the University of Vermont College of Medicine and the Medical Center Hospital of Vermont are seeking a psychiatrist for its adult Inpatient Psychiatry Services. The position carries with it a full-time faculty appointment. The position is structured so as to provide time for teaching and research activities.

The MCHV, in Burlington, Vermont, is the major teaching hospital of the College of Medicine. It is a primary referral center for the local region and a tertiary referral center for Vermont, northern New England, and New York.

Applicants should be board-eligible and have prior experience in similar inpatient settings. Applications will be accepted until the position is filled. Applicants should send a letter and curriculum vitae to:

John E. Helzer, M.D.
Professor and Chairman
Department of Psychiatry
University of Vermont College of Medicine
Burlington, Vermont 05405

The University of Vermont is an affirmative action and equal opportunity employer. Women and minorities are encouraged to apply.

## CHIEF, PSYCHIATRY SERVICE

***THE ATLANTA VETERANS ADMINISTRATION MEDICAL CENTER*** **is currently recruiting for a Chief, Psychiatry Services position.**

Available January 1991. Emory University-affiliated general medial and surgery hospital with well-established affiliated residency training program in all major specialties. The Psychiatry Services consist of 48 psychiatry beds plus 48 substance abuse beds; an outpatient or Mental Health Clinic as well as a Day Hospital and Day Treatment program with strong emphasis on clinical as well as medical training. This is a key leadership position within our department.

Credentials should include board certification in psychiatry, administrative experience and/or training, strong leadership activities, an interest in clinical psychiatry as well as an interest in teaching and research.

Opportunities exist for independent or collaborative research with excellent research facilities. Clinical practice and consultation opportunities are available through our faculty group practice plan at the Emory Clinic.

If interested and qualified, please submit a letter and curriculum vitae to: **Donald Manning, M.D., Professor and Vice Chairman, Department of Psychiatry, Emory University School of Medicine, P.O. Box AF, Atlanta, GA 30322.** AA/EOE.

## FELLOWSHIPS

The Department of Psychiatry at the University of Oklahoma Medical Center is offering one- and two-year fellowships in substance abuse and cross cultural psychiatry for PGY-4 or PGY-5 psychiatric physicians. Core training includes inpatient and consultation; outpatient programs; advanced training includes teaching, administration, and research.

Send correspondence including research and three letters of reference to:

Joseph Westermeyer, M.D., Ph.D., Chair
Department of Psychiatry
University of Oklahoma Medical Center
P.O. Box 26901 - 5SP 530
Oklahoma City, OK 73190.

The University of Oklahoma is an affirmative action/Equal Opportunity Employer.
If you would like further information, call Sarah Suemnick at (405) 271-6425.

## AMERICAN PSYCHIATRIC ASSOCIATION'S

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Could you use the APA's assistance in planning, improving services or solving a problem at your hospital or facility?

This long-standing program of the APA provides **confidential** consultations to all mental health care organizations on topics ranging from low utilization of beds to disagreement among staff about methods of treatment.

We will provide a focused consultation **tailored to meet your specific needs.** Our professional consultants are outstanding psychiatrists and experts in other related disciplines. Our reasonable fees make the Consultation Service a **cost-effective** way to help resolve your organization's problems.

**For more information contact:**

Ms. Susan Kuper
Consultation Service
American Psychiatric Association
1400 K Street, N.W.
Washington, DC 20005
(202) 682-6203

*All inquiries remain confidential.*

## PSYCHIATRIST

An additional position is immediately available for a board-certified or board-eligible psychiatrist at the Veterans Administration Medical Center, Highland Drive, Pittsburgh, PA to run an acute admission unit and supervise residents. Highland Drive is a Neuropsychiatric Medical Center affiliated with the University of Pittsburgh. Faculty appointment is available to qualified applicants.

Active teaching programs include supervision of psychiatric residents from Western Psychiatric Institute and Clinic, University of Pittsburgh. The facility offers a full-range of psychiatry treatment and specialized programs including:

- **Day Treatment**
- **Inpatient and Outpatient Substance Abuse Treatment Programs**
- **Mental Hygiene Clinic**
- **Consultation/Liaison**
- **Geriatrics**
- **Sleep Evaluation Center**
- **Neurobehavioral Unit**
- **and Schizophrenia Research Unit.**

Research is encouraged and supported. Excellent supporting staff with a multidisciplinary team approach.

Licensure in any state required. Excellent fringe benefits, including special pay in addition to salary and 30 days paid vacation per year for full-time physicians.

***Send C.V. to:***
***Jeffrey L. Peters, M.D., Chief of Psychiatry Service***
***Veterans Administration Medical Center, Highland Drive***
***Pittsburgh, PA 15206***
***or call (412) 365-4484 or 365-4483***

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## Assistant Professor Position Division of Child Psychiatry

The Division of Child Psychiatry and Child Psychiatry and Child Development, Department of Psychiatry and Behavioral Sciences at Stanford University School of Medicine seeks a child psychiatrist to participate in its research, clinical and teaching programs in pervasive developmental disorders.

We are especially interested in expanding our emphasis on molecular neurobiology, in particular how genes regulate the development and function of the central nervous system. We have an active and established program in molecular neurobiology of CNS receptors and enzymes and a strong collaborative effort in molecular genetics in severe developmental disorders. We seek a child psychiatrist with experience in molecular biology to interact with existing academic programs and to develop research and clinical programs in autism and related developmental disorders.

The position requires an M.D. and board eligibility/certification in child psychiatry. Candidates should have an advanced or equivalent training/experience in molecular biology, molecular neurobiology or molecular genetics, and have a demonstrated interest in and commitment to research, teaching and clinical service in pervasive developmental disorders. This is a tenure-track position at Stanford University at the Assistant Professor level.

Stanford University is committed to increasing representation of women and members of minority groups on its faculty and particularly encourages applications from such candidates. Applicants should forward a curriculum vitae and the names of three referees within four weeks of the date of publication of this advertisement to: **Dr. Roland Ciaranello, Chairman of the Search Committee, c/o Department of Psychiatry and Behavioral Sciences, Stanford Medical Center, Stanford, CA 94305-1028.**

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## DALHOUSIE UNIVERSITY
## DEPARTMENT OF PSYCHIATRY
## DIVISION OF CHILD PSYCHIATRY
## Child Psychiatry Vacancy

The Division of Child Psychiatry is seeking a fully qualified child psychiatrist for a full-time academic position. This position includes active staff membership at the Izaak Walton Killam Children's Hospital, Halifax, Nova Scotia.

Academic duties would include teaching undergraduate and postgraduate trainees and participating in continuing medical education. Active research interests would be an asset.

Clinical duties would largely be with outpatients and may include community consultation. Depending on seniority, the incumbent might assume direction of psychiatric outpatient services at the Izaak Walton Killam Children's Hospital. A small private practice is negotiable.

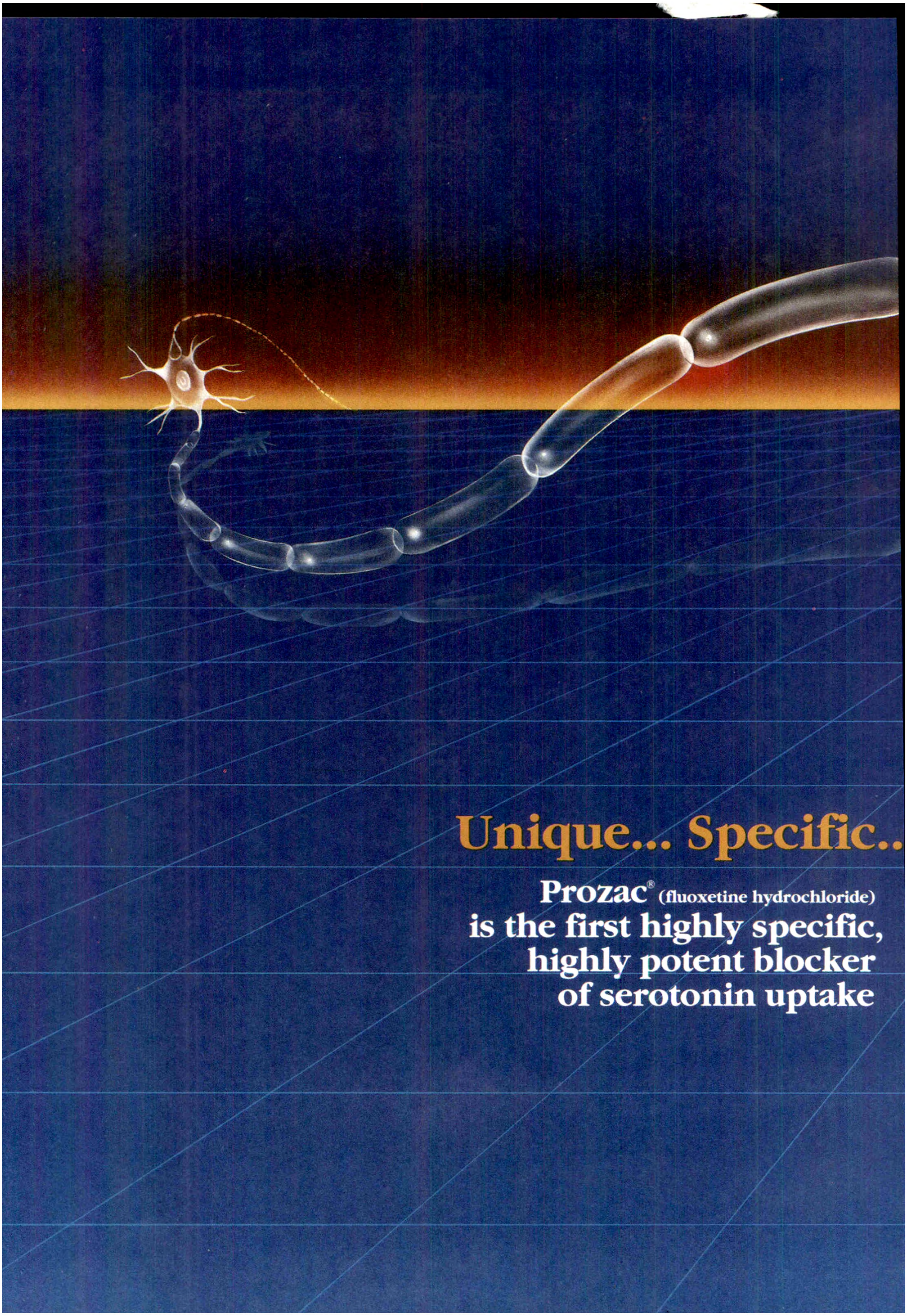
There is opportunity for further development of an academic child psychiatry service. The child mental health service delivery system in Nova Scotia is under active review and new directions for child psychiatry are being planned with the potential of modernizing and expanding these services.

Qualifications for the position are the F.R.C.P.C. or equivalent in psychiatry, full member status in the Canadian Academy of Child Psychiatry, and a current license to practice in Nova Scotia.

"Dalhousie University has a policy of affirmative action in hiring qualified women academic staff and in accordance with Canadian immigration requirements, priority will be given to Canadian citizens and permanent residents."

Interested candidates should write, including an updated curriculum vitae to:

*Dr. A. Munro, Head*
*Dalhousie University*
*Department of Psychiatry*
*Camp Hill Medical Centre*
*4th Floor - Lane Building*
*1763 Robie Street*
*Halifax, Nova Scotia B3H 3G2*
*Canada*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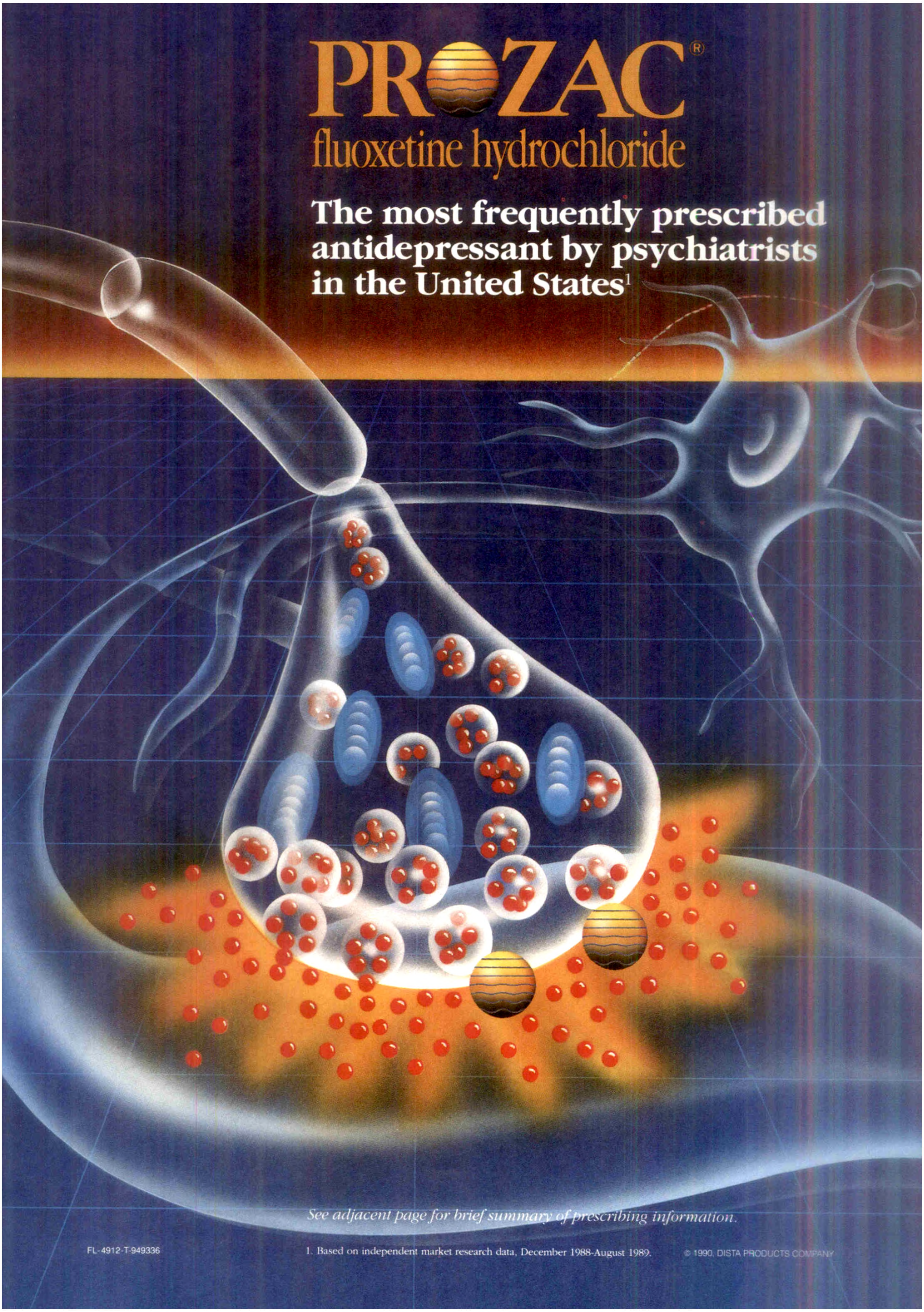

**PROZAC®**

fluoxetine hydrochloride

**The most frequently prescribed antidepressant by psychiatrists in the United States[1]**

*See adjacent page for brief summary of prescribing information.*

FL-4912-T-949336

[1] Based on independent market research data, December 1988-August 1989.

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# **Prozac**®(fluoxetine hydrochloride)

**Brief Summary:**
**Consult the package literature for complete information.**

**Indications:** Prozac is indicated for the treatment of depression.

**Contraindication:** Prozac is contraindicated in patients known to be hypersensitive to it.

**Warnings:** *Monoamine Oxidase Inhibitors* — Data on the effects of the combined use of fluoxetine and MAO inhibitors are limited. Their combined use should be avoided. Based on experience with the combined administration of MAOIs and tricyclics, at least 14 days should elapse between discontinuation of an MAO inhibitor and initiation of treatment with fluoxetine.

Because of the long half-lives of fluoxetine and its active metabolite, at least five weeks (approximately five half-lives of norfluoxetine) should elapse between discontinuation of fluoxetine and initiation of therapy with an MAOI. Administration of an MAOI within five weeks of discontinuation of fluoxetine may increase the risk of serious events. While a causal relationship to fluoxetine has not been established, death has been reported to occur following the initiation of MAOI therapy shortly after discontinuation of fluoxetine.

*Rash and Accompanying Events* — During premarketing testing of more than 5,600 US patients given fluoxetine, approximately 4% developed a rash and/or urticaria. Among these cases, almost a third were withdrawn from treatment because of the rash and/or systemic signs or symptoms associated with the rash. Clinical findings reported in association with rash include fever, leukocytosis, arthralgias, edema, carpal tunnel syndrome, respiratory distress, lymphadenopathy, proteinuria, and mild transaminase elevation. Most patients improved promptly with discontinuation of fluoxetine and/or adjunctive treatment with antihistamines or steroids, and all patients experiencing these events were reported to recover completely.

Two patients are known to have developed a serious cutaneous systemic illness. In neither patient was there an unequivocal diagnosis, but one was considered to have a leukocytoclastic vasculitis, and the other, a severe desquamating syndrome that was considered variously to be a vasculitis or erythema multiforme. Several other patients have had systemic syndromes suggestive of serum sickness.

Since the introduction of Prozac, systemic events, possibly related to vasculitis, have developed in patients with rash. Although these events are rare, they may be serious, involving the lung, kidney, or liver. Death has been reported to occur in association with these systemic events.

Whether these systemic events and rash have a common underlying cause or are due to different etiologies or pathogenic processes is not known. Upon the appearance of rash, Prozac should be discontinued.

**Precautions:** *General* — Anxiety and Insomnia — Anxiety, nervousness, and insomnia were reported by 10% to 15% of patients treated with Prozac. These symptoms led to drug discontinuation in 5% of patients treated with Prozac.

Altered Appetite and Weight — Significant weight loss, especially in underweight depressed patients, may be an undesirable result of treatment with Prozac.

In controlled clinical trials, approximately 9% of patients treated with Prozac experienced anorexia. This incidence is approximately sixfold that seen in placebo controls. A weight loss of greater than 5% of body weight occurred in 13% of patients treated with Prozac compared to 4% of placebo- and 3% of tricyclic-antidepressant-treated patients. However, only rarely have patients been discontinued from treatment with Prozac because of weight loss.

Activation of Mania/Hypomania — During premarketing testing, hypomania or mania occurred in approximately 1% of fluoxetine-treated patients. Activation of mania/hypomania has also been reported in a small proportion of patients with Major Affective Disorder treated with other marketed antidepressants.

Seizures — Twelve patients among more than 6,000 evaluated worldwide in the course of premarketing development of fluoxetine experienced convulsions (or events described as possibly having been seizures), a rate of 0.2% that appears to be similar to that associated with other marketed antidepressants. Prozac should be introduced with care in patients with a history of seizures.

Suicide — The possibility of a suicide attempt is inherent in depression and may persist until significant remission occurs. Close supervision of high-risk patients should accompany initial drug therapy. Prescriptions for Prozac should be written for the smallest quantity of capsules consistent with good patient management, in order to reduce the risk of overdose.

The Long Elimination Half-Lives of Fluoxetine and Its Metabolites — Because of the long elimination half-lives of the parent drug (two to three days) and its major active metabolite (seven to nine days), changes in dose will not be fully reflected in plasma for several weeks, affecting both strategies for titration to final dose and withdrawal from treatment (*see* Clinical Pharmacology *and* Dosage and Administration).

Use in Patients With Concomitant Illness — Clinical experience with Prozac in patients with concomitant systemic illness is limited. Caution is advisable in using Prozac in patients with diseases or conditions that could affect metabolism or hemodynamic responses.

Fluoxetine has **not** been evaluated or used to any appreciable extent in patients with a recent history of myocardial infarction or unstable heart disease. Patients with these diagnoses were systematically excluded from clinical studies during the product's premarket testing. However, the electrocardiograms of 312 patients who received Prozac in double-blind trials were retrospectively evaluated; no conduction abnormalities that resulted in heart block were observed. The mean heart rate was reduced by approximately three beats/min.

In subjects with cirrhosis of the liver, the clearances of fluoxetine and its active metabolite, norfluoxetine, were decreased, thus increasing the elimination half-lives of these substances. A lower or less frequent dose should be used in patients with cirrhosis.

Since fluoxetine is extensively metabolized, excretion of unchanged drug in urine is a minor route of elimination. However, until adequate numbers of patients with severe renal impairment have been evaluated during chronic treatment with fluoxetine, it should be used with caution in such patients.

In patients with diabetes, Prozac may alter glycemic control. Hypoglycemia has occurred during therapy with Prozac, and hyperglycemia has developed following discontinuation of the drug. As is true with many other types of medication when taken concurrently by patients with diabetes, insulin and/or oral hypoglycemic dosage may need to be adjusted when therapy with Prozac is instituted or discontinued.

Interference With Cognitive and Motor Performance — Any psychoactive drug may impair judgment, thinking, or motor skills, and patients should be cautioned about operating hazardous machinery, including automobiles, until they are reasonably certain that the drug treatment does not affect them adversely.

*Information for Patients* — Physicians are advised to discuss the following issues with patients for whom they prescribe Prozac:

Because Prozac may impair judgment, thinking, or motor skills, patients should be advised to avoid driving a car or operating hazardous machinery until they are reasonably certain that their performance is not affected.

Patients should be advised to inform their physician if they are taking or plan to take any prescription or over-the-counter drugs or alcohol.

Patients should be advised to notify their physician if they become pregnant or intend to become pregnant during therapy.

Patients should be advised to notify their physician if they are breast feeding an infant.

Patients shoud be advised to notify their physician if they develop a rash or hives.

*Laboratory Tests* — There are no specific laboratory tests recommended.

*Drug Interactions* — As with all drugs, the potential for interaction by a variety of mechanisms (ie, pharmacodynamic, pharmacokinetic drug inhibition or enhancement, etc) is a possibility (*see* Accumulation and Slow Elimination *under* Clinical Pharmacology).

Tryptophan — Five patients receiving Prozac in combination with tryptophan experienced adverse reactions, including agitation, restlessness, and gastrointestinal distress.

Monoamine Oxidase Inhibitors — *See* Warnings.

Other Antidepressants — There have been greater than twofold increases of previously stable plasma levels of other antidepressants when Prozac has been administered in combination with these agents (*see* Accumulation and Slow Elimination *under* Clinical Pharmacology).

Lithium — There have been reports of both increased and decreased lithium levels when lithium was used concomitantly with fluoxetine. Cases of lithium toxicity have been reported. Lithium levels should be monitored when these drugs are administered concomitantly.

Diazepam Clearance — The half-life of concurrently administered diazepam may be prolonged in some patients (*see* Accumulation and Slow Elimination *under* Clinical Pharmacology).

Potential Effects of Coadministration of Drugs Highly Bound to Plasma Proteins — Because fluoxetine is tightly bound to plasma protein, the administration of fluoxetine to a patient taking another drug that is tightly bound to protein (eg, Coumadin, digitoxin) may cause a shift in plasma concentrations potentially resulting in an adverse effect. Conversely, adverse effects may result from displacement of protein-bound fluoxetine by other tightly bound drugs (*see* Accumulation and Slow Elimination *under* Clinical Pharmacology).

CNS-Active Drugs — The risk of using Prozac in combination with other CNS-active drugs has not been systematically evaluated. Consequently, caution is advised if the concomitant administration of Prozac and such drugs is required (*see* Accumulation and Slow Elimination *under* Clinical Pharmacology).

Electroconvulsive Therapy — There are no clinical studies establishing the benefit of the combined use of ECT and fluoxetine. A single report of a prolonged seizure in a patient on fluoxetine has been reported.

*Carcinogenesis, Mutagenesis, Impairment of Fertility* — There is no evidence of carcinogenicity, mutagenicity, or impairment of fertility with Prozac.

The dietary administration of fluoxetine to rats and mice for two years at levels equivalent to approximately 7.5 and 9.0 times the maximum human dose (80 mg) respectively produced no evidence of carcinogenicity.

Fluoxetine and norfluoxetine have been shown to have no genotoxic effects based on the following assays: bacterial mutation assay, DNA repair assay in cultured rat hepatocytes, mouse lymphoma assay, and in vivo sister chromatid exchange assay in Chinese hamster bone marrow cells.

Two fertility studies conducted in rats at doses of approximately five and nine times the maximum human dose (80 mg) indicated that fluoxetine had no adverse effects on fertility. A slight decrease in neonatal survival was noted, but this was probably associated with depressed maternal food consumption and suppressed weight gain.

*Pregnancy* — Teratogenic Effects — Pregnancy Category B — Reproduction studies have been performed in rats and rabbits at doses nine and 11 times the maximum daily human dose (80 mg) respectively and have revealed no evidence of harm to the fetus due to Prozac. There are, however, no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

*Labor and Delivery* — The effect of Prozac on labor and delivery in humans is unknown.

*Nursing Mothers* — Because many drugs are excreted in human milk, caution should be exercised when Prozac is administered to a nursing woman. In one breast milk sample, the concentration of fluoxetine plus norfluoxetine was 70.4 ng/mL. The concentration in the mother's plasma was 295.0 ng/mL. No adverse effects on the infant were reported.

*Usage in Children* — Safety and effectiveness in children have not been established.

*Usage in the Elderly* — Prozac has not been systematically evaluated in older patients; however, several hundred elderly patients have participated in clinical studies with Prozac, and no unusual adverse age-related phenomena have been identified. However, these data are insufficient to rule out possible age-related differences during chronic use, particularly in elderly patients who have concomitant systemic illnesses or who are receiving concomitant drugs.

*Hyponatremia* — Several cases of hyponatremia (some with serum sodium lower than 110 mmol/L) have been reported. The hyponatremia appeared to be reversible when Prozac was discontinued. Although these cases were complex with varying possible etiologies, some were possibly due to the syndrome of inappropriate antidiuretic hormone secretion (SIADH). The majority of these occurrences have been in older patients and in patients taking diuretics or who were otherwise volume depleted.

**Adverse Reactions:** *Commonly Observed* — The most commonly observed adverse events associated with the use of Prozac and not seen at an equivalent incidence among placebo-treated patients were: nervous system complaints, including anxiety, nervousness, and insomnia; drowsiness and fatigue or asthenia; tremor; sweating; gastrointestinal complaints, including anorexia, nausea, and diarrhea; and dizziness or lightheadedness.

*Associated With Discontinuation of Treatment* — Fifteen percent of approximately 4,000 patients who received Prozac in US premarketing clinical trials discontinued treatment due to an adverse event. The more common events causing discontinuation included: psychiatric (5.3%), primarily nervousness, anxiety, and insomnia; digestive (3.0%), primarily nausea; nervous system (1.6%), primarily dizziness; body as a whole (1.5%), primarily asthenia and headache; and skin (1.4%), primarily rash and pruritus.

*Incidence in Controlled Clinical Trials* — The table that follows enumerates adverse events that occurred at a frequency of 1% or more among Prozac-treated patients who participated in controlled trials comparing Prozac with placebo. The prescriber should be aware that these figures cannot be used to predict the incidence of side effects in the course of usual medical practice where patient characteristics and other factors differ from those that prevailed in the clinical trials. Similarly, the cited frequencies cannot be compared with figures obtained from other clinical investigations involving different treatments, uses and investigators. The cited figures, however, do provide the prescribing physician with some basis for estimating the relative contribution of drug and nondrug factors to the side-effect incidence rate in the population studied.

TREATMENT-EMERGENT ADVERSE EXPERIENCE INCIDENCE
IN PLACEBO-CONTROLLED CLINICAL TRIALS

| Body System/ Adverse Event* | Percentage of Patients Reporting Event | | Body System/ Adverse Event* | Percentage of Patients Reporting Event | |
|---|---|---|---|---|---|
| | Prozac (N = 1,730) | Placebo (N = 799) | | Prozac (N = 1,730) | Placebo (N = 799) |
| **Nervous** | | | **Body as a Whole** | | |
| Headache | 20.3 | 15.5 | Asthenia | 4.4 | 1.9 |
| Nervousness | 14.9 | 8.5 | Infection, viral | 3.4 | 3.1 |
| Insomnia | 13.8 | 7.1 | Pain, limb | 1.6 | 1.1 |
| Drowsiness | 11.6 | 6.3 | Fever | 1.4 | — |
| Anxiety | 9.4 | 5.5 | Pain, chest | 1.3 | 1.1 |
| Tremor | 7.9 | 2.4 | Allergy | 1.2 | 1.1 |
| Dizziness | 5.7 | 3.3 | Influenza | 1.2 | 1.5 |
| Fatigue | 4.2 | 1.1 | **Respiratory** | | |
| Sedated | 1.9 | 1.3 | Upper respiratory infection | 7.6 | 6.0 |
| Sensation disturbance | 1.7 | 2.0 | Flu-like syndrome | 2.8 | 1.9 |
| Libido, decreased | 1.6 | — | Pharyngitis | 2.7 | 1.3 |
| Light-headedness | 1.6 | — | Nasal congestion | 2.6 | 2.3 |
| Concentration, decreased | 1.5 | — | Headache, sinus | 2.3 | 1.8 |
| **Digestive** | | | Sinusitis | 2.1 | 2.0 |
| Nausea | 21.1 | 10.1 | Cough | 1.6 | 1.6 |
| Diarrhea | 12.3 | 7.0 | Dyspnea | 1.4 | — |
| Mouth dryness | 9.5 | 6.0 | **Cardiovascular** | | |
| Anorexia | 8.7 | 1.5 | Hot flushes | 1.8 | 1.0 |
| Dyspepsia | 6.4 | 4.3 | Palpitations | 1.3 | 1.4 |
| Constipation | 4.5 | 3.3 | **Musculoskeletal** | | |
| Pain abdominal | 3.4 | 2.9 | Pain, back | 2.0 | 2.4 |
| Vomiting | 2.4 | 1.3 | Pain, joint | 1.2 | 1.1 |
| Taste change | 1.8 | — | Pain, muscle | 1.2 | 1.0 |
| Flatulence | 1.6 | 1.1 | **Urogenital** | | |
| Gastroenteritis | 1.0 | 1.4 | Menstruation, painful | 1.9 | 1.4 |
| **Skin and Appendages** | | | Sexual dysfunction | 1.9 | — |
| Sweating, excessive | 8.4 | 3.8 | Frequent micturition | 1.6 | — |
| Rash | 2.7 | 1.8 | Urinary tract infection | 1.2 | — |
| Pruritus | 2.4 | 1.4 | **Special Senses** | | |
| | | | Vision disturbance | 2.8 | 1.8 |

*Events reported by at least 1% of Prozac-treated patients are included
— Incidence less than 1%

*Other Events Observed During the Premarketing Evaluation of Prozac* — During clinical testing in the US, multiple doses of Prozac were administered to approximately 5,600 subjects. Untoward events associated with this exposure were recorded by clinical investigators using descriptive terminology of their own choosing. Consequently, it is not possible to provide a meaningful estimate of the proportion of individuals experiencing adverse events without first grouping similar types of untoward events into a limited (ie, reduced) number of standardized event categories.

In the tabulations which follow, a standard COSTART Dictionary terminology has been used to classify reported adverse events. The frequencies presented, therefore, represent the proportion of the 5,600 individuals exposed to Prozac who experienced an event of the type cited on at least one occasion while receiving Prozac. All reported events are included except those already listed in tables, those COSTART terms so general as to be uninformative, and those events where a drug cause was remote. It is important to emphasize that, although the events reported did occur during treatment with Prozac, they were not necessarily caused by it.

Events are further classified within body system categories and enumerated in order of decreasing frequency using the following definitions: frequent adverse events are defined as those occuring on one or more occasions in at least 1/100 patients; infrequent adverse events are those occurring in 1/100 to 1/1,000 patients; rare events are those occurring in less than 1/1,000 patients.

Body as a Whole — *Frequent:* chills; *Infrequent:* chills and fever, cyst, face edema, hangover effect, jaw pain, malaise, neck pain, neck rigidity, and pelvic pain; *Rare:* abdomen enlarged, cellulitis, hydrocephalus, hypothermia, LE syndrome, moniliasis, and serum sickness.

Cardiovascular System — *Infrequent:* angina pectoris, arrhythmia, hemorrhage, hypertension, hypotension, migraine, postural hypotension, syncope, and tachycardia; *Rare:* AV block first-degree, bradycardia, bundle-branch block, cerebral ischemia, myocardial infarct, thrombophlebitis, vascular headache, and ventricular arrhythmia.

Digestive System — *Frequent:* increased appetite; *Infrequent:* aphthous stomatitis, dysphagia, eructation, esophagitis, gastritis, gingivitis, glossitis, liver function tests abnormal, melena, stomatitis, thirst; *Rare:* bloody diarrhea, cholecystitis, cholelithiasis, colitis, duodenal ulcer, enteritis, fecal incontinence, hematemesis, hepatitis, hepatomegaly, hyperchlorhydria, increased salivation, jaundice, liver tenderness, mouth ulceration, salivary gland enlargement, stomach ulcer, tongue discoloration, and tongue edema.

Endocrine System — *Infrequent:* hypothyroidism; *Rare:* goiter and hyperthyroidism.

Hemic and Lymphatic System — *Infrequent:* anemia and lymphadenopathy; *Rare:* bleeding time increased, blood dyscrasia, leukopenia, lymphocytosis, petechia, purpura, sedimentation rate increased, and thrombocythemia.

Metabolic and Nutritional — *Frequent:* weight loss; *Infrequent:* generalized edema, hypoglycemia, peripheral edema, and weight gain; *Rare:* dehydration, gout, hypercholesteremia, hyperglycemia, hyperlipemia, hypoglycemic reaction, hypokalemia, hyponatremia, and iron deficiency anemia.

Musculoskeletal System — *Infrequent:* arthritis, bone pain, bursitis, tenosynovitis, and twitching; *Rare:* bone necrosis, chondrodystrophy, muscle hemorrhage, myositis, osteoporosis, pathological fracture, and rheumatoid arthritis.

Nervous System — *Frequent:* abnormal dreams and agitation; *Infrequent:* abnormal gait, acute brain syndrome, akathisia, amnesia, apathy, ataxia, buccoglossal syndrome, CNS stimulation, convulsion, delusions, depersonalization, emotional lability, euphoria, hallucinations, hostility, hyperkinesia, hypesthesia, incoordination, libido increased, manic reaction, neuralgia, neuropathy, paranoid reaction, psychosis, and vertigo; *Rare:* abnormal electroencephalogram, antisocial reaction, chronic brain syndrome, circumoral paresthesia, CNS depression, coma, dysarthria, dystonia, extrapyramidal syndrome, hypertonia, hysteria, myoclonus, nystagmus, paralysis, reflexes decreased, stupor, and torticollis.

Respiratory System — *Frequent:* bronchitis, rhinitis, and yawn; *Infrequent:* asthma, epistaxis, hiccup, hyperventilation, and pneumonia; *Rare:* apnea, hemoptysis, hypoxia, larynx edema, lung edema, lung fibrosis/alveolitis, and pleural effusion.

Skin and Appendages — *Infrequent:* acne, alopecia, contact dermatitis, dry skin, herpes simplex, maculopapular rash, and urticaria; *Rare:* eczema, erythema multiforme, fungal dermatitis, herpes zoster, hirsutism, psoriasis, purpuric rash, pustular rash, seborrhea, skin discoloration, skin hypertrophy, subcutaneous nodule, and vesiculobullous rash.

Special Senses — *Infrequent:* amblyopia, conjunctivitis, ear pain, eye pain, mydriasis, photophobia, and tinnitus; *Rare:* blepharitis, cataract, corneal lesion, deafness, diplopia, eye hemorrhage, glaucoma, iritis, ptosis, strabismus, and taste loss.

Urogenital System — *Infrequent:* abnormal ejaculation, amenorrhea, breast pain, cystitis, dysuria, fibrocystic breast, impotence, leukorrhea, menopause, menorrhagia, ovarian disorder, urinary incontinence, urinary retention, urinary urgency, urination impaired, and vaginitis; *Rare:* abortion, albuminuria, breast enlargement, dyspareunia, epididymitis, female lactation, hematuria, hypomenorrhea, kidney calculus, metrorrhagia, orchitis, polyuria, pyelonephritis, pyuria, salpingitis, urethral pain, urethritis, urinary tract disorder, urolithiasis, uterine hemorrhage, uterine spasm, and vaginal hemorrhage.

*Postintroduction Reports* — Voluntary reports of adverse events temporarily associated with Prozac that have been received since market introduction and which may have no causal relationship with the drug include the following: vaginal bleeding after drug withdrawal, hyperprolactinemia, thrombocytopenia, and confusion.

**Overdosage:** *Human Experience* — As of December 1987, there were two deaths among approximately 38 reports of acute overdose with fluoxetine, either alone or in combination with other drugs and/or alcohol. One death involved a combined overdose with approximately 1,800 mg of fluoxetine and an undetermined amount of maprotiline. Plasma concentrations of fluoxetine and maprotiline were 4.57 mg/L and 4.18 mg/L respectively. A second death involved three drugs yielding plasma concentrations as follows: fluoxetine, 1.93 mg/L; norfluoxetine, 1.10 mg/L; codeine, 1.80 mg/L; temazepam, 3.80 mg/L.

One other patient who reportedly took 3,000 mg of fluoxetine experienced two grand mal seizures that remitted spontaneously without specific anticonvulsant treatment (*see* Management). The actual amount of drug absorbed may have been less due to vomiting.

Nausea and vomiting were prominent in overdoses involving higher fluoxetine doses. Other prominent symptoms of overdose included agitation, restlessness, hypomania, and other signs of CNS excitation. Except for the two deaths noted above, all other overdose cases recovered without residua.

Since introduction, a single death attributed to overdose of fluoxetine alone has been reported.

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**See complete prescribing information in SK&F literature or *PDR*. The following is a brief summary.**

**Contraindications:** Comatose states or presence of large amounts of C.N.S. depressants.

**Warnings: The possibility of extrapyramidal reactions from chlorpromazine may confuse the diagnosis of Reye's syndrome or other encephalopathy. Therefore, avoid use in children or adolescents with suspected Reye's syndrome.**

May cause persistent tardive dyskinesia, which appears to be irreversible in some patients. Reserve chronic neuroleptic treatment for patients with chronic illness 1) that is known to respond to neuroleptics and 2) for whom there are no safer but equally effective treatment options. Use the smallest effective dose over the shortest treatment duration. If signs and symptoms of tardive dyskinesia develop, consider discontinuing the neuroleptic. A potentially fatal symptom complex sometimes referred to as Neuroleptic Malignant Syndrome (NMS) has been reported in association with antipsychotic drugs. To manage NMS 1) discontinue immediately antipsychotic drugs and any other drugs not essential to concurrent therapy; 2) treat symptoms intensively and monitor; 3) where possible, treat serious concomitant medical problems. If antipsychotic treatment is needed after recovery from NMS, consider reintroducing drug therapy and monitor the patient carefully as recurrences of NMS have been reported. 'Thorazine' ampuls and vials contain sodium bisulfite and sodium sulfite; the sulfite may cause allergic reactions, including anaphylactic symptoms. In patients with bone marrow depression or previously demonstrated hypersensitivity (e.g., blood dyscrasias, jaundice) with phenothiazines, do not administer 'Thorazine' unless the potential treatment benefits outweigh the possible hazards. Caution patients about activities requiring alertness (e.g., operating vehicles or machinery) especially during the first few days therapy. Avoid concomitant use with alcohol. May counteract antihypertensive effect of guanethidine and related compounds. Use in pregnancy only when essential. There are reported instances of prolonged jaundice, extrapyramidal signs, hyperreflexia or hyporeflexia in newborns whose mothers had received chlorpromazine. Chlorpromazine is excreted in the breast milk of nursing mothers.

**Precautions:** Advise patients and/or guardians of the risk of tardive dyskinesia from chronic therapy. Use cautiously in persons with cardiovascular, liver, renal or chronic respiratory disease, or with acute respiratory infections. Patients with a history of hepatic encephalopathy due to cirrhosis have increased sensitivity to the C.N.S. effects of chlorpromazine. Due to cough reflex suppression, aspiration of vomitus is possible. May prolong or intensify the action of C.N.S. depressants, organophosphorus insecticides, heat, atropine and related drugs. (Reduce dosage of concomitant C.N.S. depressants.) Anticonvulsant action of barbiturates is not intensified.

Neuroleptic drugs cause elevated prolactin levels that persist during chronic administration. Since approximately one third of human breast cancers are prolactin-dependent *in vitro*, this elevation is of potential importance if neuroleptic drug administration is contemplated in a patient with a previously detected breast cancer. Neither clinical nor epidemiologic studies to date, however, have shown an association between the chronic administration of neuroleptic drugs and mammary tumorigenesis. Chromosomal aberrations in spermatocytes and abnormal sperm have been demonstrated in rodents treated with certain neuroleptics. Use cautiously in glaucoma patients. May diminish the effect of oral anticoagulants, produce α-adrenergic blockade, and lower the convulsive threshold; dosage adjustment of anticonvulsants may be required. May interfere with Dilantin®* metabolism, causing 'Dilantin' toxicity. May cause false positive phenylketonuria test results. Do not use with Amipaque®†. Discontinue 'Thorazine' at least 48 hours before myelography, do not resume for at least 24 hours postprocedure, and do not use to control N/V prior to myelography or postprocedure with 'Amipaque'. Evaluate patients with a history of long-term therapy with 'Thorazine' and/or other neuroleptics periodically to decide whether the dosage could be reduced or therapy discontinued. Antiemetic effect may mask signs of overdosage of other drugs or obscure diagnosis and treatment of conditions such as intestinal obstruction, brain tumor and Reye's syndrome (see Warnings). When used concomitantly, may obscure vomiting as a sign of toxicity of a cancer chemotherapeutic agent. Discontinue high-dose, long-term therapy gradually. Patients with a history of long-term therapy with 'Thorazine' and/or other neuroleptics should be evaluated periodically for possible adjustment or discontinuance of drug therapy.

**Adverse Reactions:** Drowsiness; cholestatic jaundice; agranulocytosis, eosinophilia, leukopenia, hemolytic anemia, aplastic anemia, thrombocytopenic purpura and pancytopenia; postural hypotension, tachycardia, fainting, dizziness and occasionally a shock-like condition; reversal of epinephrine effects; EKG changes have been reported; neuromuscular (extrapyramidal) reactions: dystonias, motor restlessness, pseudo-parkinsonism, persistent tardive dyskinesia, psychotic symptoms, catatonic-like states, cerebral edema; convulsive seizures; abnormality of the cerebrospinal fluid proteins; urticarial reactions and photosensitivity, exfoliative dermatitis, contact dermatitis; asthma, laryngeal edema, angioneurotic edema, and anaphylactoid reactions; lactation and breast engorgement (in females on large doses), false positive pregnancy tests, amenorrhea, gynecomastia; hyperglycemia, hypoglycemia, glycosuria; dry mouth, nasal congestion, constipation, adynamic ileus, urinary retention, priapism, miosis, mydriasis; after prolonged substantial doses, skin pigmentation, epithelial keratopathy, lenticular and corneal deposits and pigmentary retinopathy, visual impairment; mild fever (after large I.M. doses); hyperpyrexia; increased appetite and weight; a systemic lupus erythematosus-like syndrome; peripheral edema.

NOTE: Sudden death in patients taking phenothiazines (apparently due to cardiac arrest or asphyxia due to failure of cough reflex) has been reported but no causal relationship has been established.

**How Supplied: Tablets:** 10 mg, 25 mg or 50 mg, in bottles of 100 and 1000; in Single Unit Packages of 100 (intended for institutional use only). For use in severe neuropsychiatric conditions, 100 mg and 200 mg, in bottles of 100 and 1000; in Single Unit Packages of 100 (intended for institutional use only).

**Spansule® brand of sustained release capsules:** 30 mg, 75 mg, 150 mg or 200 mg, in bottles of 50 and 500; in Single Unit Packages of 100 (intended for institutional use only). For use in severe neuropsychiatric conditions, 300 mg, in bottles of 50; in Single Unit Packages of 100 (intended for institutional use only).

**Ampuls:** 1 mL and 2 mL (25 mg/mL), in boxes of 10, 100 and 500.

**Multiple-dose Vials:** 10 mL (25 mg/mL), in boxes of 1, 20 and 100.

**Syrup:** 10 mg/5 mL in 4 fl oz bottles.

**Suppositories:** 25 mg or 100 mg, in boxes of 12.

**Concentrate:** Intended for institutional use. 30 mg/mL, in 4 fl oz bottles and in cartons of 36 bottles. 100 mg/mL, in 8 fl oz bottles, in cartons of 12.

*phenytoin, Parke-Davis.
†metrizamide, Winthrop Pharmaceuticals.

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**By-line.** Authors listed in the by-line should be limited to principal researchers and/or writers; collaborators may be acknowledged in a footnote. Authors' first names are preferred to initials. Degrees should be included after each author's name.

**Previous presentation.** If the paper has been presented at a meeting, please give the name of the meeting, the place, and the date.

**Location of work and address for reprints.** Provide the department, institution, city, and state **where the work was done.** Include a full address for the author who is to receive reprint requests.

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### Abstract

The abstract is a single paragraph no longer than 100 words for Special Articles and Regular Articles and no longer than 40 words for Clinical and Research Reports.

### Text

Authors should use the active voice and first person; headings and subheadings should be inserted at reasonable intervals. Footnotes to text may not be used, and summaries are usually unnecessary.

**Research design and statistics.** The following information regarding research design should be included: 1) a clearly stated hypothesis, 2) the names of the statistical tests used, 3) whether tests were one- or two-tailed, and 4) what test was used for each set of data. Reporting of standard deviations, rather than standard errors of the mean, is required. Statistical tests that are not well known should be referenced. **All** significant and important nonsignificant results must include the test value, degree(s) of freedom, and probability. For example, "The analysis of variance indicated that those who abstained from coffee had significantly higher course grades than those who did not abstain ($F=4.32$, $df=3, 17$, $p<0.05$)." Reviewers will evaluate the appropriateness of the analyses.

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1. Noyes R Jr, DuPont RL Jr, Pecknold JC, et al: Alprazolam in panic disorder and agoraphobia, results from a multicenter trial, II: patient acceptance, side effects, and safety. Arch Gen Psychiatry 1988; 45:423–428
2. Kaplan HI, Sadock BJ (eds): Comprehensive Textbook of Psychiatry, 4th ed, vol 2. Baltimore, Williams & Wilkins, 1985
3. Fyer AJ, Manuzza S, Endicott J: Differential diagnosis and assessments of anxiety: recent developments, in Psychopharmacology: The Third Generation of Progress. Edited by Meltzer HY. New York, Raven Press, 1987

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### Figures

Figures are considered as text and are subject to revision by the authors upon recommendation of the Editors. Figures should, however, be professionally prepared. Glossy or other camera-ready prints should accompany the submitted manuscript. Computer-generated figures that do not meet quality printing standards will be returned for revision. The first author's name, the title of the paper, the figure number, and the top of the figure should be noted on a label affixed to the back of each figure. All figure titles and footnotes should be typed and sent together on a separate page.

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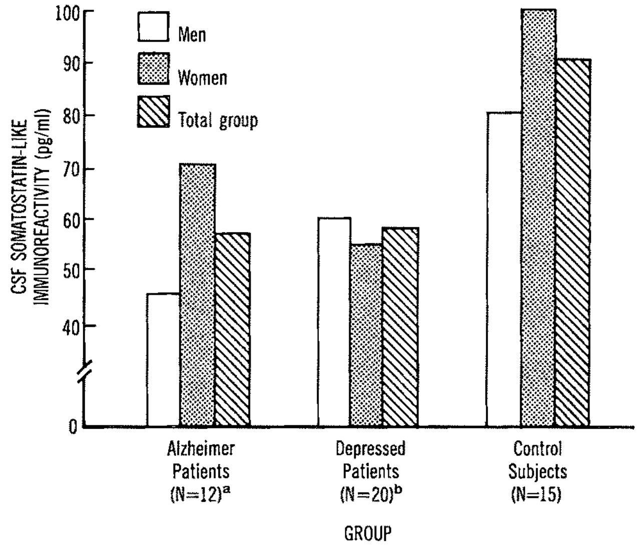
**Format.** Figures are visual expressions of data trends or relationships. Figures that represent numerical data which could be expressed more succinctly or clearly in tabular form should be converted to tables. Line graphs should show change in continuous variables; comparisons of like values in different groups should be presented as bar graphs. Graphs containing stacked bars are unacceptable; the different segments of each bar should be presented side by side.

**Lettering.** Figure type should be sans serif and should be 7 points or larger after the figure is reduced; most figures taking up the width of a vertical manuscript page are reduced to a width of 19.5 picas (3¼ inches), and those requiring a horizontal manuscript page are usually reduced to 40.5 picas (6¾ inches). When space on the horizontal axis is insuffi-

**FIGURE 1. Mean CSF Somatostatin Levels of Patients With Alzheimer's Disease, Older Depressed Patients, and Age-Matched Control Subjects**



[a] Significant difference between men and women ($t=1.81$, $df=10$, $p<0.05$) and between the total Alzheimer's disease group and the total control group ($t=2.49$, $df=25$, $p<0.01$).

[b] Significant difference between the total depressed group and the total control group ($t=2.75$, $df=33$, $p<0.005$).

cient, headings may be placed diagonally on the axis. Main headings should consist of upper-case letters only, subheadings of upper- and lower-case, and other type (e.g., keys, flow chart segments) of lower-case with only an initial upper-case letter. All parenthetical material should be lower-case. Do not use idiosyncratic abbreviations.

**Other.** The following are additional specific requirements. Please refer to the example given above.

1. Do not use solid black shading; rather, include outlined white among shadings.
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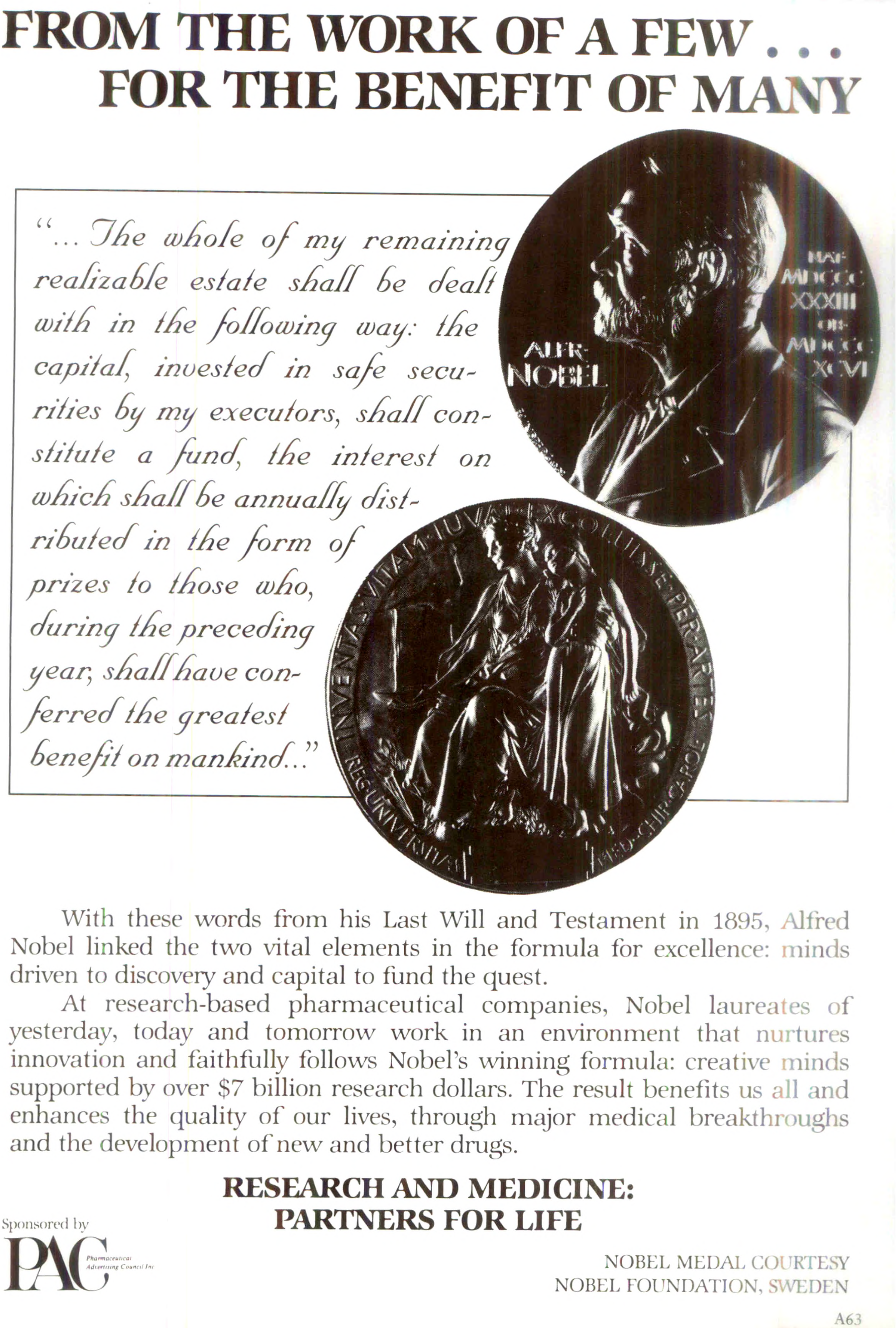
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*"... The whole of my remaining realizable estate shall be dealt with in the following way: the capital, invested in safe securities by my executors, shall constitute a fund, the interest on which shall be annually distributed in the form of prizes to those who, during the preceding year, shall have conferred the greatest benefit on mankind..."*

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## (HALOPERIDOL) INJECTION 100mg/mL

# **HALDOL® Decanoate 50**

## (HALOPERIDOL) INJECTION 50mg/mL

For IM Injection Only

**The following is a brief summary only. Before prescribing, see complete prescribing information in HALDOL and HALDOL Decanoate product labeling.**

**Contraindications:** Since the pharmacologic and clinical actions of HALDOL Decanoate 50 and HALDOL Decanoate 100 are attributed to HALDOL haloperidol as the active medication, Contraindications, Warnings, and additional information are those of HALDOL, modified to reflect the prolonged action.

HALDOL is contraindicated in severe toxic central nervous system depression or comatose states from any cause and in individuals who are hypersensitive to this drug or have Parkinson's disease.

**Warnings:** *Tardive Dyskinesia.* Tardive dyskinesia, a syndrome consisting of potentially irreversible, involuntary, dyskinetic movements may develop in patients treated with antipsychotic drugs. Although the prevalence of the syndrome appears to be highest among the elderly, especially elderly women, it is impossible to rely upon prevalence estimates to predict, at the inception of antipsychotic treatment, which patients are likely to develop the syndrome. Whether antipsychotic drug products differ in their potential to cause tardive dyskinesia is unknown. Both the risk of developing tardive dyskinesia and the likelihood that it will become irreversible are believed to increase as the duration of treatment and the total cumulative dose of antipsychotic drugs administered to the patient increase. However, the syndrome can develop, although much less commonly, after relatively brief treatment periods at low doses. There is no known treatment for established cases of tardive dyskinesia, although the syndrome may remit, partially or completely, if antipsychotic treatment is withdrawn. Antipsychotic treatment, itself, however, may suppress (or partially suppress) the signs and symptoms of the syndrome and thereby may possibly mask the underlying process. The effect that symptomatic suppression has upon the long-term course of the syndrome is unknown. Given these considerations, antipsychotic drugs should be prescribed in a manner that is most likely to minimize the occurrence of tardive dyskinesia. Chronic antipsychotic treatment should generally be reserved for patients who suffer from a chronic illness that 1) is known to respond to antipsychotic drugs, and 2) for whom alternative, equally effective, but potentially less harmful treatments are **not** available or appropriate. In patients who do require chronic treatment, the smallest dose and the shortest duration of treatment producing a satisfactory clinical response should be sought. The need for continued treatment should be reassessed periodically. If signs and symptoms of tardive dyskinesia appear in a patient on antipsychotics, drug discontinuation should be considered. However, some patients may require treatment despite the presence of the syndrome. (For further information about the description of tardive dyskinesia and its clinical detection, please refer to ADVERSE REACTIONS.)

*Neuroleptic Malignant Syndrome (NMS).* A potentially fatal symptom complex sometimes referred to as Neuroleptic Malignant Syndrome (NMS) has been reported in association with antipsychotic drugs. Clinical manifestations of NMS are hyperpyrexia, muscle rigidity, altered mental status (including catatonic signs) and evidence of autonomic instability (irregular pulse or blood pressure, tachycardia, diaphoresis, and cardiac dysrhythmias). Additional signs may include elevated creatine phosphokinase, myoglobinuria (rhabdomyolysis) and acute renal failure. The diagnostic evaluation of patients with this syndrome is complicated. In arriving at a diagnosis, it is important to identify cases where the clinical presentation includes both serious medical illness (e.g., pneumonia, systemic infection, etc.) and untreated or inadequately treated extrapyramidal signs and symptoms (EPS). Other important considerations in the differential diagnosis include central anticholinergic toxicity, heat stroke, drug fever and primary central nervous system (CNS) pathology. The management of NMS should include 1) immediate discontinuation of antipsychotic drugs and other drugs not essential to concurrent therapy, 2) intensive symptomatic treatment and medical monitoring, and 3) treatment of any concomitant serious medical problems for which specific treatments are available. There is no general agreement about specific pharmacological treatment regimens for uncomplicated NMS. If a patient requires antipsychotic drug treatment after recovery from NMS, the potential reintroduction of drug therapy should be carefully considered. The patient should be carefully monitored, since recurrences of NMS have been reported. Hyperpyrexia and heat stroke, not associated with the above symptom complex, have also been reported with HALDOL.

*Usage in Pregnancy* (see PRECAUTIONS—Usage in Pregnancy). *Combined Use With Lithium* (see PRECAUTIONS—Drug Interactions).

*General.* Bronchopneumonia, sometimes fatal, has followed use of antipsychotic drugs, including haloperidol. Prompt remedial therapy should be instituted if dehydration, hemoconcentration or reduced pulmonary ventilation occur, especially in the elderly. Decreased serum cholesterol and/or cutaneous and ocular changes have been reported with chemically-related drugs, although not with haloperidol. See PRECAUTIONS—Information for Patients for information on mental and/or physical abilities and on concomitant use with other substances.

**Precautions:** Administer cautiously to patients: (1) with severe cardiovascular disorders, due to the possibility of transient hypotension and/or precipitation of anginal pain (if a vasopressor is required, epinephrine should not be used since HALDOL may block its vasopressor activity and paradoxical further lowering of blood pressure may occur; metaraminol, phenylephrine or norepinephrine should be used); (2) receiving anticonvulsant medications, with a history of seizures, or with EEG abnormalities, because HALDOL may lower the convulsive threshold. If indicated, adequate anticonvulsant therapy should be concomitantly maintained; (3) with known allergies or a history of allergic reactions to drugs; (4) receiving anticoagulants, since an isolated instance of interference occurred with the effects of one anticoagulant (phenindione). Concomitant antiparkinson medication, if required, may have to be continued after HALDOL is discontinued because of different excretion rates; if both are discontinued simultaneously, extrapyramidal symptoms may occur. Intraocular pressure may increase when anticholinergic drugs, including antiparkinson drugs, are administered concomitantly with HALDOL. When HALDOL is used for mania in bipolar disorders, there may be a rapid mood swing to depression. Severe neurotoxicity may occur in patients with thyrotoxicosis receiving antipsychotic medication, including HALDOL.

The 1, 5, 10 mg HALDOL tablets contain FD&C Yellow No. 5 (tartrazine) which may cause allergic-type reactions (including bronchial asthma) in certain susceptible individuals, especially in those who have aspirin hypersensitivity.

*Information for Patients.* Mental and/or physical abilities required for hazardous tasks or driving may be impaired. Alcohol should be avoided due to possible additive effects and hypotension.

*Drug Interactions.* Patients receiving lithium plus haloperidol should be monitored closely for early evidence of neurological toxicity and treatment discontinued promptly if such signs appear. As with other antipsychotic agents, it should be noted that HALDOL may be capable of potentiating CNS depressants such as anesthetics, opiates, and alcohol.

*Carcinogenesis, Mutagenesis and Impairment of Fertility.* No mutagenic potential of haloperidol decanoate was found in the Ames Salmonella microsomal activation assay.

Carcinogenicity studies using oral haloperidol were conducted in Wistar rats (dosed at up to 5 mg/kg daily for 24 months) and in Albino Swiss mice (dosed at up to 5 mg/kg daily for 18 months). In the rat study survival was less than optimal in all dose groups, reducing the number of rats at risk for developing tumors. However, although a relatively greater number of rats survived to the end of the study in high dose male and female groups, these animals did not have a greater incidence of tumors than control animals. Therefore, although not optimal, this study does suggest the absence of a haloperidol related increase in the incidence of neoplasia in rats at doses up to 20 times the usual daily human dose for chronic or resistant patients. In female mice at 5 and 20 times the highest initial daily dose for chronic or resistant patients, there was a statistically significant increase in mammary gland neoplasia and total tumor incidence; at 20 times the same daily dose there was a statistically significant increase in pituitary gland neoplasia. In male mice, no statistically significant differences in incidences of total tumors or specific tumor types were noted.

Antipsychotic drugs elevate prolactin levels; the elevation persists during chronic administration. Tissue culture experiments indicate that approximately one-third of human breast cancers are prolactin dependent *in vitro*, a factor of potential importance if the prescription of these drugs is contemplated in a patient with a previously detected breast cancer. Although disturbances such as galactorrhea, amenorrhea, gynecomastia, and impotence have been reported, the clinical significance of elevated serum prolactin levels is unknown for most patients. An increase in mammary neoplasms has been found in rodents after chronic administration of antipsychotic drugs. Neither clinical studies nor epidemiologic studies conducted to date, however, have shown an association between chronic administration of these drugs and mammary tumorigenesis; the available evidence is considered too limited to be conclusive at this time.

*Usage in Pregnancy.* Pregnancy Category C. Safe use in pregnancy or in women likely to become pregnant has not been established; use only if benefit clearly justifies potential hazards to the fetus.

*Nursing Mothers.* Infants should not be nursed during drug treatment.

*Pediatric Use.* Controlled trials to establish the safety and effectiveness of intramuscular administration in children have not been conducted.

**Adverse Reactions:** Adverse reactions following the administration of HALDOL Decanoate 50 or HALDOL Decanoate 100 are those of HALDOL haloperidol. Since vast experience has accumulated with HALDOL, the adverse reactions are reported for that compound as well as for haloperidol decanoate. As with all injectable medications, local tissue reactions have been reported with haloperidol decanoate.

*CNS Effects. Extrapyramidal Reactions*—Neuromuscular (extrapyramidal) reactions have been reported frequently, often during the first few days of treatment. Generally they involved Parkinson-like symptoms which when first observed were usually mild to moderately severe and usually reversible. Other types of neuromuscular reactions (motor restlessness, dystonia, akathisia, hyperreflexia, opisthotonos, oculogyric crises) have been reported far less frequently, but were often more severe. Severe extrapyramidal reactions have been reported at relatively low doses. Generally, extrapyramidal symptoms are dose-related since they occur at relatively high doses and disappear or become less severe when the dose is reduced. Antiparkinson drugs may be required. Persistent extrapyramidal reactions have been reported and the drug may have to be discontinued in such cases. *Withdrawal Emergent Neurological Signs*—Abrupt discontinuation of short-term antipsychotic therapy is generally uneventful. However, some patients on maintenance treatment experience transient dyskinetic signs after abrupt withdrawal. In certain cases these are indistinguishable from "Tardive Dyskinesia" except for duration. It is unknown whether gradual withdrawal will reduce the occurrence of these signs, but until further evidence is available HALDOL should be gradually withdrawn. *Tardive Dyskinesia*—As with all antipsychotic agents, HALDOL has been associated with persistent dyskinesias. Tardive dyskinesia, a syndrome consisting of potentially irreversible, involuntary, dyskinetic movements, may appear in some patients on long-term therapy or may occur after drug therapy has been discontinued. The risk appears to be greater in elderly patients on high-dose therapy, especially females. The symptoms are persistent and in some patients irreversible. The syndrome is characterized by rhythmical involuntary movements of tongue, face, mouth or jaw (e.g., protrusion of tongue, puffing of cheeks, puckering of mouth, chewing movements). Sometimes these may be accompanied by involuntary movements of extremities and the trunk. There is no known effective treatment for tardive dyskinesia; antiparkinson agents usually do not alleviate the symptoms of this syndrome. It is suggested that all antipsychotic agents be discontinued if these symptoms appear. Should it be necessary to reinstitute treatment, or increase the dosage of the agent, or switch to a different antipsychotic agent, this syndrome may be masked. It has been reported that fine vermicular movement of the tongue may be an early sign of tardive dyskinesia and if the medication is stopped at that time the full syndrome may not develop. *Tardive Dystonia*—Tardive dystonia, not associated with the above syndrome, has also been reported. Tardive dystonia is characterized by delayed onset of choreic or dystonic movements, is often persistent, and has the potential of becoming irreversible. *Other CNS Effects*—Insomnia, restlessness, anxiety, euphoria, agitation, drowsiness, depression, lethargy, headache, confusion, vertigo, grand mal seizures, and exacerbation of psychotic symptoms including hallucinations, and catatonic-like behavioral states which may be responsive to drug withdrawal and/or treatment with anticholinergic drugs.

*Body as a Whole:* Neuroleptic malignant syndrome (NMS), hyperpyrexia and heat stroke have been reported with HALDOL. (See WARNINGS for further information concerning NMS.) *Cardiovascular Effects.* Tachycardia, hypotension, hypertension and ECG changes. *Hematologic Effects.* Reports of mild, usually transient leukopenia and leukocytosis, minimal decreases in red blood cell counts, anemia, or a tendency toward lymphomonocytosis; agranulocytosis rarely reported and only in association with other medication. *Liver Effects.* Impaired liver function and/or jaundice. *Dermatologic Reactions.* Maculopapular and acneiform reactions, isolated cases of photosensitivity, loss of hair. *Endocrine Disorders.* Lactation, breast engorgement, mastalgia, menstrual irregularities, gynecomastia, impotence, increased libido, hyperglycemia, hypoglycemia and hyponatremia. *Gastrointestinal Effects.* Anorexia, constipation, diarrhea, hypersalivation, dyspepsia, nausea and vomiting. *Autonomic Reactions.* Dry mouth, blurred vision, urinary retention, diaphoresis, and priapism. *Respiratory Effects.* Laryngospasm, bronchospasm and increased depth of respiration. *Special Senses.* Cataracts, retinopathy and visual disturbances. *Other.* Cases of sudden and unexpected death have been reported in association with the administration of HALDOL. The nature of the evidence makes it impossible to determine definitively what role, if any, HALDOL played in the outcome of the reported cases. The possibility that HALDOL caused death cannot, of course, be excluded, but it is to be kept in mind that sudden and unexpected death may occur in psychotic patients when they go untreated or when they are treated with other antipsychotic drugs.

**IMPORTANT: Full directions for use should be read before HALDOL or HALDOL Decanoate products are administered or prescribed.**

**For information on symptoms and treatment of overdosage, see full prescribing information.**

The short-acting HALDOL injectable form is intended only for acutely agitated psychotic patients with moderately severe to very severe symptoms.

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(HALOPERIDOL) INJECTION 100mg/mL
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Volume 147, Number 3    March 1990

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Toward a Clinical Model of Psychotherapy for Depression, II: An Integrative and Selective Treatment Approach

By T. Byram Karasu

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*Studies of the Epidemiology of Bulimia Nervosa*
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*A Debate:*

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*Implications of* Osheroff v. Chestnut Lodge
By Gerald L. Klerman

*Law, Science, and Psychiatric Malpractice:*
*A Response to Klerman's Indictment of Psychoanalytic Psychiatry*
By Alan A. Stone

# *Books Received*

**Psychotherapy and Character Structure: How to Recognize and Treat Particular Character Types,** by Mary Ahern, M.S.W., Ph.D., and A.J. Malerstein, M.D. New York, Human Sciences Press (Plenum), 1989, 249 pp., no price listed.

**Dirty Words: Psychoanalytic Insights,** by Ariel C. Arango, M.D. Northvale, N.J., Jason Aronson, 1989, 219 pp., $20.00.

**Brain Power: Unlock the Power of Your Mind,** edited by Prof. J. Graham Beaumont. New York, Salem House (Harper & Row), 1989, 253 pp., $24.95.

**Being a Widow** (1988), by Lynn Caine. New York, Penguin Books, 1990, 249 pp., $7.95 (paper).

**Alzheimer's Disease: Treatment and Long-Term Management,** edited by Jeffrey L. Cummings and Bruce L. Miller. New York, Marcel Dekker, 1990, 380 pp., $125.00.

**Contemporary Themes in Psychiatry: A Tribute to Sir Martin Roth,** edited by Kenneth Davison and Alan Kerr. London, Gaskell (Royal College of Psychiatrists), 1989, 506 pp., £20.00 (paper).

**Health and Medicine in the Hindu Tradition: Continuity and Cohesion,** by Prakash N. Desai. New York, Crossroad, 1989, 144 pp., $19.95.

**Holiday of Darkness: A Psychologist's Personal Journey Out of His Depression, revised ed.,** by Norman S. Endler. Toronto, Wall & Thompson, 1990, 149 pp., $9.95 (paper).

**Thinking Fragments: Psychoanalysis, Feminism, and Postmodernism in the Contemporary West,** by Jane Flax. Berkeley, University of California Press, 1990, 265 pp., $25.00.

**Alcohol and the Writer** (1988), by Donald W. Goodwin, M.D. New York, Penguin Books, 1989, 210 pp., $8.95 (paper).

**Group Processes in Therapeutic Communities,** by Sigmund Karterud, M.D. Oslo, Sigmund Karterud, 1989, unnumbered pages, no price listed (paper).

**Perspectives on Animal Research, vol. 1, 1989,** edited by Stephen R. Kaufman, M.D., and Betsy Todd, R.N. New York, Medical Research Modernization Committee, 1989, 134 pp., no price listed.

**Neuroscience in Israel,** by Naomi Oren, M.D., Ph.D., and Oded Abramsky, M.D., Ph.D. Jerusalem, Israeli Ministry of Science and Technology, 1989, 331 pp., no price listed (paper).

**Psychiatric Diagnostic Interview, Revised (PDI-R),** by Ekkehard Othmer, M.D., Ph.D., Elizabeth C. Penick, Ph.D., Barbara J. Powell, Ph.D., Marsha R. Read, Ph.D., ACSW, and Sieglinde C. Othmer, Ph.D. Los Angeles, Western Psychological Services, 1989, 561 pp., no price listed (paper) (manual and administration booklet).

**The Craft of Psychotherapy: Twenty-Seven Studies,** by I.H. Paul, Ph.D. Northvale, N.J., Jason Aronson, 1989, 293 pp., $30.00.

**On Becoming a Health and Human Services Manager: A Practical Guide for Clinicians and Counselors,** by Paul G. Quinnett. New York, Continuum, 1989, 210 pp., $19.95.

**The Future of Mental Health Services Research: DHHS Publication ADM-89-1600,** edited by Carl A. Taube, Ph.D., David Mechanic, Ph.D., and Ann A. Hohmann, Ph.D., M.P.H. Rockville, Md., National Institute of Mental Health, 1989, 324 pp., no price listed (paper).

**Le Principe d'Existence: Un Devenir Psychiatrique de la Phénoménologie,** by Serge Valdinoci. Norwell, Mass., Kluwer Academic, 1989, 164 pp., $73.00.

**Behaviour Problems in Children: Orthodox and Paradox in Therapy,** by Robert Wilkins, M.B., M.R.C.P., M.R.C.Psych. Oxford, Heinemann Nursing (Stoneham, Mass., Butterworths, distributor), 1989, 139 pp., $39.95 (paper).

**The Seat of the Soul,** by Gary Zukov. New York, Fireside (Simon & Schuster), 1989, 248 pp., $8.95 (paper).

THE AMERICAN JOURNAL OF PSYCHIATRY
*Special Articles*

# A Description of Eating Disorders in 1932

Albert Stunkard, M.D.

*This article consists of a shortened and annotated translation of a paper on "An Interesting Oral Symptom Complex and Its Relationship to Addiction" by M. Wulff of Berlin, which was delivered before the German Psychoanalytic Society on April 12, 1932. The article describes four cases of an eating disorder in women that was characterized by binge eating, hypersomnolence, apathetic depression, and disparagement of the body image. After the eating binges, all four patients manifested periods of fasting, and two of the three, about whom such information is available, vomited. Translations of large excerpts of the case histories are presented together with a summary of Wulff's discussion.*

(Am J Psychiatry 1990; 147:263–268)

The following is a biographical note on Moshe Wulff. Wulff was born in Odessa in 1878 and studied medicine in Berlin. In 1908 he met Karl Abraham, who introduced him to psychoanalysis, and he soon became a dedicated proponent (E. Gumbel, personal communication, April 20, 1988). In 1909 he was dismissed from his position in Berlin because of his "Freudian views" (1, p. 76) and returned to Odessa, since "Russia . . . was then a freer country than Germany in such matters" (1, p. 110). From Odessa he continued his contact with Abraham and corresponded with both Freud and Ferenczi. In 1910, according to Kurt Eissler, he accompanied the Wolf-Man from his home in Odessa to Vienna and introduced him to Freud (personal communication, Jan. 21, 1988). In 1914 Wulff moved to Moscow, where he taught psychoanalysis, and in 1917, he became docent and the first psychoanalyst in the Faculty of Medicine of the University of Moscow (E. Gumbel, personal communication). Jones mentions Wulff and Ossipow as "those most worthy of remembrance in connection with the early days—and as it was to prove, also the last days—of psychoanalysis in Russia" (1, p. 76).

In 1927 Wulff returned to Berlin, where he worked in Simmel's psychoanalytic sanitarium. In 1933 he moved to Tel Aviv, where he practiced psychoanalysis until his death in 1971. He was a founder and, for 10 years (1943–1953), the President of the Israel Psychoanalytic Society. According to a colleague, Wulff was "a good clinician, excellent teacher and productive writer. He did never undergo a personal analysis" (E. Gumbel, personal communication).

It is widely believed that bulimia is a modern disease. Unlike anorexia nervosa, for which a rich history has been traced to the Middle Ages (2), bulimia seems to have burst from the blue upon modern society, and it has achieved widespread recognition in a very short period of time. A new publication, *The International Journal of the Eating Disorders*, is devoted to bulimia (and anorexia nervosa), and successive estimates of the prevalence of bulimia have risen to a peak of 19% of college women (3). Interest in bulimia in the popular press has risen in parallel. Personal accounts have filled the pages of women's magazines, and *Newsweek* magazine pronounced 1981 as "The Year of the Binge-Purge Syndrome" (4). Is it possible that such a distinctive disorder could have arisen de novo in the past decade?

Bulimia is probably not a new disorder. The evidence is of two types—scattered historical references compatible with bulimia over the past 250 years and three detailed case histories in the past 50 years. Either source alone would be insufficient to make the case. Together they barely do. It therefore seems useful to

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publish a translation of a paper by Wulff published in 1932 that described in considerable detail four cases of a disorder that appears similar to current descriptions of bulimia (5).

The scattered historical references have been reported by Stein and Laakso (6). They noted that as long ago as 1743, James described "true boulimus," which was characterized by intense preoccupation with food and overeating at very short intervals, followed by fainting, and a variant, *caninus appetitus*, in which the overeating was terminated by vomiting (7). This account was followed in 1785 by that of Motherby, who distinguished three types of bulimia—bulimia of the pure hunger type, bulimia associated with "swooning," and that terminated by vomiting (8). The disorder was sufficiently well-recognized to warrant an entry in the 1797 edition of the *Encyclopedia Britannica*.

The only nineteenth-century reference compatible with current concepts appears to be that of Blachez in 1869, who described two forms of "boulimie" (9). In each, food might become the major preoccupation of the person, hunger might persist even after the consumption of enormous amounts of food, and torpor might follow the binge. In the subtype called cynorexia, the eating binge was followed by vomiting. It is worthy of note that Gull's 1874 description of anorexia nervosa included the occasional occurrence of an extremely voracious appetite (10).

Bulimia attracted little attention until well into the present century, although in 1903 Janet described four patients (of a total of 236 in his book) who may have been bulimic (11). In their translation and comment on these cases, Pope and associates (12) noted that these four patients overate in association with other psychiatric disorders—depression (N=2), anorexia (N=1), and agoraphobia (N=1). Vomiting was described in the case of only one patient, the only man, and the one whose binge eating was described in the most ambiguous manner—"an often voracious appetite, given to peculiar fluctuations. The patient with anorexia nervosa, a severe obsessive, also has typical disturbances of the body image."

Modern interest in bulimia first appeared in connection with patients who suffered also from anorexia nervosa. In 1950 Nemiah reported the case histories of 14 patients with this diagnosis who had been seen on the psychiatric service of the Massachusetts General Hospital over a period of 12 years (13). Four of these patients had episodes of "abnormal eating" compatible with bulimia. One subject (patient 9) presented a classic picture of bulimia nervosa, in which eating binges were followed by vomiting, as often as once a day. Vomiting was not reported among the other three subjects (patients 1, 8, and 10), but they manifested clear eating binges.

The three detailed case histories to which reference has been made were those of Binswanger's "Case of Ellen West" in 1928 (14), Lindner's case of Laura, first published in 1950 (15), and Stunkard's case of T.T. in 1959 (16). The paper that forms the basis of this report has generally escaped notice during the recent increased interest in bulimia and has received only passing notice—in Fenichel's *The Psychoanalytic Theory of Neurosis* (17). This paper, "An Interesting Oral Symptom Complex and Its Relationship to Addiction," by M. Wulff, contained not only detailed case histories but also some speculations about the nature of the disorder that, while dated in some ways, sound surprisingly modern in others.

A few notes about the translation are in order. The paper has been shortened to about one-third of its original length. I have retained much of the clinical descriptions but have summarized the lengthy theoretical discussion. As was apparently the custom, this discussion, complete with assertions of certainty such as "without doubt" and "unquestionably," was interspersed among the clinical descriptions. I have omitted short descriptions of two male patients whose clinical pictures differed substantially from those of the four female patients.

I have provided verbatim accounts in a literal translation that includes some redundancies, in an effort to capture the flavor of this fascinating period piece. Although Wulff included extensive verbatim statements that supposedly were made by the patients, it is difficult to imagine people talking in this way, even in Berlin in 1932. It seems unlikely that they were taken from the author's notes, since, as he remarked at the end of the paper, most of his notes had been lost. Similarly, it is unclear if the often hyperbolic descriptions of patient behavior were based on observations by Wulff, as he often implies, or were simply his acceptance of the patients' accounts, as seems more likely. There is, for example, no corroboration of the account of a patient who "could eat one after another three or four meals of three or four courses each and in between them sweets, chocolate and cookies by the poundful."

One final note. The German language contains two words for eating—*essen* (by people) and *fressen* (by animals). The patients in Wulff's account frequently referred to their eating as "fressen," and to call attention to this special meaning, it is translated as "eating like an animal." The original text follows.

## TRANSLATION OF WULFF'S PAPER

The clinical picture to be described consists of a symptom complex that always appears at the same time or in a certain order, and that, as far as I know, has never before been described. My first observation of this symptom complex occurred nearly 16 years ago. Since then I have been able to observe three further cases . . . . I will now describe in words a picture of this condition in which the symptom complex is particularly clearly depicted, as was told to me by one of my patients, a 20-year-old woman student.

Case A: "I don't always eat in the same way. Sometimes there occurs to me a particular mental state and then I eat a great deal. I call this condition the 'spiritually degenerate condition of a person who has fallen to a low moral level.' As soon as I begin to eat very much I am possessed by a bad mood, deep despair and hopelessness, apathetic indifference, complete loss of will, no desires, no joy. I don't work, become completely apathetic and very sleepy. I eat a great deal and sleep a great deal, almost all day long. And then I become very fat, as if swollen, as if edematous. My appearance changes, I look completely different. I don't want to get dressed and wear only old dirty clothes, preferably only an old bathrobe, don't comb my hair, wash very little and insufficiently. At such times my room is a terrible mess; everything is in confusion; nothing is put away; washing, clothes, books, and various articles lie everywhere in chaotic disorder. In this condition eating is an unconquerable passion to which I succumb and that I cannot fight against. I have compared myself to an alcoholic, an addict. Sweets and baked goods have a particularly powerful attraction for me . . . . "

The condition began for the first time to a pronounced degree when the patient was 15 years old and continued thereafter fairly chronically. The patient was very fat then, obese; menstruation was scanty and irregular, and physicians assumed that it was an endocrine disorder. The condition improved with time; it recurred periodically from time to time, remained at first for some months, then for shorter periods of time, sometimes for only a few days, even for only one day. "Any kind of failure, an illness, an affront, loss of self-confidence can lead to this condition. Then there appears also a tormenting feeling of inferiority and a strong disgust with myself, of my own body; I appear to myself as dirty, loathsome, repulsive." In this condition the patient is irritable and full of hatred toward her surroundings, toward everyone.

The condition can suddenly disappear and give way to a heightened feeling of self: "One evening it is completely unbearable—and the next morning I get up as if transformed, don't know why, and feel that I am fresh, lively, energetic; I feel well. Then I eat very little. In a very good spiritual condition I eat absolutely nothing; then I feel particularly good, lively, in an elevated mood and eat nothing, even though I am hungry. However, if I once eat my fill, there follows remorse, anxiety, and despondency; I feel that once again I have fallen to a low moral level, believe that I have spoiled everything, promise myself that I will never do it again. I make a powerful effort of will to come out of this condition, and I am in complete despair if I am not successful! And I remain in this condition as long as I am not able to abstain from food, thereby freeing myself from these tormenting feelings and bringing back the good elevated condition of abstinence . . . . "

Case B: The second case concerns a severe hysteric with . . . a very large number of other symptoms, which I will not recount here. Among these other symptoms eating disorders are clearly in the first rank . . . .

The following situation was repeated daily for several months: Within a few minutes after eating the patient would become very upset, her face red and puffy, her eyes shone, her appearance agitated; the upset increased so that she could neither sit nor remain calm; conversation with her became impossible because she could not listen. Then a severe headache followed, particularly in one place on her skull, precisely in the middle (an hysterogenous zone), strong feelings of sickness and vomiting. After vomiting, a certain calm began, but the headache became stronger until it led to unconsciousness; the patient fell into an unconscious condition and underwent an attack. In order to avoid this—which was only occasionally successful—the patient attempted to keep food intake to a minimum in good periods and did not touch many kinds of foods, particularly bread, puddings, and pulpy foods; she ate primarily raw fruit, eventually a small piece of meat. When she was alone in her room, in particular, frequently between meals, she would secretly take some fruit as if she were stealing—and she was best able to retain this.

There also occurred periods of differing duration—from a few days up to three weeks—in which the picture suddenly changed. The patient called these "circumstances of animal eating," in which she had a drive to eat that was impossible to withstand. At these times she devoured everything edible that she could reach and would not become at all full. She did not vomit but retained the food. In these circumstances, in contrast to her usual food intake, she was able to consume enormous amounts of food and at the height of this condition would consume even inedible objects such as orange peels, fruit cores, even scraps of paper and similar things if she could not find anything else. Her eating appeared to be that of greedy eating like an animal . . . . It was no longer possible to recognize the beautiful, thin 20-year-old girl during these days; mostly she lay in bed behind closed windows and quickly covered her face with her hand when someone came into the room. She remained all day long unwashed and unkempt in a dirty, loose dressing gown. From time to time she got out of bed and walked around the room bent over, as if bowing, with a puffy, swollen, somewhat edematous face, a gloomy, despairing look on her face, with her bowels knotted together and her glance directed toward the floor. Often she did not speak all day long and quickly averted her face, as if she wanted to hide, when anyone came into the room.

At such times she had a particularly strong feeling of disgust toward her own body. If she let her hand fall even very lightly on her body she twitched full of disgust and pulled it back quickly with a look on her face as if she had disturbed something terrible, dirty, and disgusting; at such times she would often say "disgusting." Looking at her own body and its outlines through her clothes was so painful to her that she could tolerate only a very loose nightgown so that the outline of her body was not visible. She liked best to wear a wide coat or a large shawl; at night she did not get undressed but remained in her bathrobe and coat. This feeling of disgust toward her own body also began in this patient in puberty, when she was 13 to 14 years old, and the first signs of a female body form and her breasts, in particular, became noticeable. She bound herself with a towel under her clothes so tightly that she could hardly breathe. This feeling of disgust was closely connected with strong feelings of shame. These feelings of shame and of disgust were concentrated on her face and particularly strongly on her abdomen, in addition to her breasts. During an eating episode her abdomen was very blown up, and when she walked it stuck out so far that she looked exactly like a woman in her fourth or fifth month of pregnancy. Her vertebrae became bent forward in the form of a pronounced kyphoscoliosis. It was remarkable, however, that this condition could disappear without a trace fairly quickly, sometimes even overnight; but sometimes it would also fade away in the course of four or five days. The onset of menstruation often appeared to favor the disappearance of the condition.

This condition of "eating like an animal" gave way to a good condition that could last for a few days; then the patient would get up early in the morning refreshed and in good spirits, would wash and dress herself, was lovable and sometimes even in a remarkably cheerful mood. At such times she ate very little, sometimes only coffee and a little bit of fruit all day until evening, and at night slept hardly more than two or three hours. But then one day she could no longer control herself, ate a great deal at one time, retained her food, and at this point the other condition began again.

Case C: The third case concerned a bright, intelligent, well-educated woman of more than 30 years of age, a mother with two children. After a separation from her husband, it was necessary for her to support herself and her children, and her profound social incompetence was exposed . . . . In this woman there also appeared the typical picture of the symptom complex that has been described, although in an attenuated and more chronic form. She also had periods of a greedy passion to eat and sleep, accompanied by all of the psychic picture described above: dysphoria, dull apathy, irritability, carelessness in her expression. She could sit for hours in her bathrobe, hair uncombed, unwashed, almost completely motionless, lost in reverie, brooding, not knowing herself which thoughts were preoccupying her, in a dirty, disorderly room in which her clothing, books, pieces of paper, food remnants, etc. lay around; or she lay for many hours in a peculiar, deep, tormented kind of sleep. Only food was able to arouse her from this apathetic, depressed psychic state. At such times she would eat greedily and quickly wolf down whatever there was that was edible upon the table, right out of the paper in which it had been wrapped, particularly things that she liked but was not supposed to eat because of her obesity, such as sweets, pastries, bread, and so forth; and she had to think as she was doing it, "This is good; the worse, the better!" This lasted until every available edible thing had been devoured. Then there appeared again the depression, the apathetic indifference, self-loathing, reverie, and finally the tormented sleep that brought no rest or refreshment. And finally—self-reproaches, remorse, despair, and the promise never to do it again. Any kind of pleasant event, a success, could very quickly bring the patient out of this condition. Then she was energetic, lively, her mood cheerful and elevated; she happily felt a return of her ability to work; her room, clothes, the things in her wardrobe, the books would all be tidied up; then she opened up a great deal to her environment and was even vain and flirtatious. However, she limited her food intake a great deal "to take off weight." Usually, however, that did not last very long, and the slightest misfortune was sufficient to lead once again to another condition of "eating like an animal."

Case D: The fourth case concerns a young woman in her middle twenties who, since her earliest childhood—since she was 7 years old—suffered from a compulsive neurosis. [After a long description of a bizarre childhood upbringing and of "countless love affairs," Wulff went on to state the following.] The symptom complex that interests us here was developed to its fullest after her separation from her husband, which means after her failed attempt at a normal sexual life; periods of strong drives to eat that lasted for up to three weeks alternated with short, three- to six-day-long periods of abstinence that could extend to complete fasts for the entire day. The amount of food that was devoured in the course of the day, particularly in the afternoons and evenings, was sometimes unbelievable. She could eat one after the other three or four meals of three or four courses each and in between them sweets, chocolate, and cookies by the poundful. Sometimes there was an almost unbroken greedy eating of every available food, with a particular preference for sweets and carbohydrates; she particularly liked to buy anything edible that was being sold on the street and to swallow them rapidly and greedily on the spot. She ate, moreover, in such a manner that she could hardly breathe; her abdomen protruded then, and she liked to show it with the observation, "Look how much I am like a pregnant woman!" Often her eating ended with severe abdominal pain and vomiting, but immediately thereafter she ate again and even more.

Her mental condition during the periods of eating was dreadful; despair overcame her: "As if now everything is lost, my whole life has now lost its value, impossible, completely impossible, to live any longer now; I will always be loathsome like this, dirty, spoiled, turned into an animal, and I can never again be a human being. I feel disgust for myself, feel soiled, and in order to be clean I would have to take a lot of castor oil . . . . I feel fat, so fat, and that is frightening . . . . " In this condition the flirtatious woman was extremely negligent about her appearance; she took no baths, hardly washed her face and hands, rarely combed her hair, wore only old dirty clothes, slept in her clothes without taking them off so as not to see her body, not to touch herself, and not to feel anything; even when it was very hot she had to go out on the street in a large dark coat "so that people cannot see my disgusting fat body" [exactly like patient B]. During this time she also slept a great deal, but her sleep was not refreshing, and instead very restless and tormented. In these circumstances, which she called "swine conditions," she was indifferent to everyone, uninterested, psychologically alienated and empty, and accessible only to sexual arousal; yes, precisely in these times she experienced all of her love affairs: "All of my love affairs come out of this condition of mine. In those times when I do not eat I can give up rendez-vous; that doesn't interest me then and I also can't be attractive, interesting, charming. Because of that, after a three-day fast, I have a feeling of inner cleanliness . . . . "

The circumstances of her addictive eating were released primarily through some insult, particularly in her erotic affairs, when, for example, a young man from her host of admirers let her notice his indifference. Then she felt that she was ugly, repulsive, disgusting because she was fat and big and then began to eat out of spite, as she said, "out of feelings of revenge": "If I am not loved because I am like this, good; now more than ever, I will be completely bestial, completely disgusting, completely dirty, and I will do what is harmful, what is forbidden, that is, eat a great deal."

## WULFF'S DISCUSSION

Wulff's discussion ranged widely throughout the paper, interspersed with the clinical descriptions as noted earlier. Much of it is of primarily historical interest, for example, the discussion of the role of the female castration complex. I have omitted such sections and have summarized the remaining theoretical considerations but will begin with a brief summary of the clinical picture in Wulff's words.

> If in my description up until now I have perhaps drawn out the clinical material in somewhat more detailed fashion than it may seem necessary and have not avoided some repetition, I did this in order to impress more sharply the special picture of this symptom complex; thereby we saw that this symptom complex is not tied to any particular known clinical picture of illness, but occurs in different neuroses, certainly having modified the character of the basic neuroses.... Despite the ... different clinical pictures of this peculiar symptom complex—compulsive, greedy eating, the drive to sleep, apathetic depression, loathing of one's own corporeality—the clinical picture and the course of the illness were uniformly governed by a certain periodicity, even though the basic character of the clinical picture varied greatly. One gets the impression that we are dealing here with a complex of morbid clinical pictures that do not belong at all in the framework of a typical neurotic structure, but rather display a peculiar pathological alteration of important biological functions that can appear in different forms of neurotic types.

Wulff defined the clinical syndrome in terms of four behaviors—binge eating, hypersomnolence, apathetic depression, and disparagement of the body image. Its onset occurred during adolescence, except for patient C, in whom it occurred after the age of 30. Although not listed by Wulff in his summary, the question of purging can be answered by the case histories. After eating binges, all of the patients fasted and two (patients B and D) vomited. Patient A did not vomit, and there is no information about vomiting by patient C.

Much of Wulff's theoretical discussion focused upon the relationship of the syndrome to addiction, melancholia, and compulsive neurosis. He was convinced that the syndrome did not represent a compulsive neurosis, and he cited two reasons. First, he stated that a compulsion represents the breakthrough of an unacceptable inhibited drive toward a substitute object, and he saw the disturbed eating not as an unacceptable drive but as a form of oral satisfaction in a severely regressed person. Second, he stated that the repression of a compulsion should lead to anxiety, whereas in these patients control of their eating led not to anxiety but to an increase in the pressure to eat, a pressure that he termed "addictive desires." Wulff then turned to his primary concern, the differential diagnosis between addiction and melancholia, noting that he believed that the syndrome "is something between melancholia and addiction." He described its relationship to each condition, at first appearing to favor melancholia: "The condition is to be viewed as a neurotic modification of the unconscious processes of melancholia." The two conditions had in common, he believed, their precipitation by "a loss of love ... an insult to the patient's narcissism," which led to a depressed mood out of which the eating binges emerged. The eating binges, however, in his view, did not represent the oral incorporation characteristic of the melancholic patient, with "oral sadism leading to eating as annihilation." Instead, "because the object is not ambivalently regarded" (as would presumably be the case in melancholia), the eating constituted "regression to a pure oral erotic satisfaction ... almost a sexual perversion."

Wulff believed that an interpretation of eating binges as addictive was strengthened by the somnolence that followed them, "a kind of sleep drunkenness," which stood in stark contrast to the insomnia of the melancholic patient. In fact, he ascribed particular importance to this somnolence, contending that such sleep during the digestion that followed the eating binges "is as responsible as is oral erotic stimulation for the instinctual initiation of the drive to eat." He saw a kind of positive reinforcement of eating binges by an "alimentary orgasm" (18), "the libidinal investment of the entire digestive process which extends then to the entire body just as do the reactive feelings of disgust that follow."

Wulff argued that, despite the fact that the eating binges appeared to be more oral erotic than oral sadistic, the superego was evidently not entirely dissuaded from what appeared to it as a forbidden activity—oral incorporation of the penis. Accordingly, in a kind of compromise, the superego took its revenge, not in the form of a full-blown attack of melancholia, but instead in an attack on the body image, eliciting the profound disgust with their bodies that was seen in these patients. By drastic restriction of their eating the patients were able to placate the superego and escape from the depression and the associated body image disparagement. But in these "good periods," the patients "bring the same feeling of disgust to food or even to the act of eating itself," which, Wulff noted, "is understandable if we consider that what is eaten is a symbolic substitute for the disgusting, dirty but, at the same time, highly desired penis." He closed his discussion with a description that, despite its special language, has a certain modern quality.

> As soon as the superego is able to overcome the instinctual eating addiction there occurs an inner satisfaction, a peacefulness and feeling of well-being.... In this phase the patients are able, although only transiently, and at the cost of almost completely giving up an important life function, to raise themselves to the normal genital stage. The price—if at all possible, not to eat anything more—is, however, too high; it would cost one's life, if normal hunger did not reassert itself, as a result of which this effort at self-treatment can succeed only to a limited extent and must in the end miscarry. For the first reexperiencing of strong feelings of satiation brings with it the satisfaction of the alimentary orgasm and its unfailing consequences—and the whole situation begins again.

## TRANSLATOR'S DISCUSSION

Rereading Wulff's paper in preparing this translation aroused in me much of the excitement that I had felt when I first read it 40 years ago, but with a difference. At that time his case histories seemed to describe people of another era, the flamboyant hysteric patients of Charcot's Paris and Freud's Vienna. Since then I have known the kind of patients whom Wulff was describing, and his account, which had once seemed so exotic, now appeared to be, instead, careful clinical description. In fact, I was struck with the quality of the description. How many of us today, encountering such a strange and heretofore unknown disorder, could have described in such detail so many of what we have come to see as its major elements. The contrast between Wulff's case histories and our current rating-scaled descriptions of patients provides in microcosm an example of the atrophy of a set of once-valued clinical skills. We no longer make these kinds of observations, and, if we did, it is not clear where they could be published.

Wulff's report makes it clear that bulimia is not the peculiarly modern disorder that it has sometimes seemed. Eating disorders of a type similar to modern bulimia existed in revolutionary Moscow and in Berlin just before Hitler's seizure of power in 1933. The fact that bulimia could be recognized half a century ago gives added credence to the occasional earlier reports extending back over the past two centuries. There are clearly differences between these reports and modern descriptions, but these differences may be no greater than those between recent versions of APA's *Diagnostic and Statistical Manual.* These latter differences are so great that a recent study found little overlap between *DSM-III* and *DSM-III-R* criteria for bulimia: Only a minority of persons who met the criteria in either edition met the criteria in both editions (19).

If bulimia could be recognized in the past, why was it recognized so rarely? It may have been less common, it may have been underreported, or both. It seems quite possible that bulimia was less common in earlier periods. The prevalence of some behavioral disorders has fluctuated widely over time, a notable example being hysteria, which appears to be far less common now than in earlier days. Bulimia may also have been underreported. Although one might expect such a distinctive disorder to have been recognized, particular social circumstances may have led to lesser attention to it. If underreported in the past, it is probably overreported today, with, as noted earlier, reports of a prevalence as high as 19% (3). Recent careful studies, by contrast, have found clinically significant bulimia in less than 2% of college women (19, 20).

A virtue of careful clinical descriptions from the past is the perspective they provide on clinical problems in the present. An example is the light thrown on one popular modern explanation for bulimia—the feminist critique—as exemplified particularly in Orbach's *Fat Is a Feminist Issue* (21). Placing strong emphasis on the predominance of bulimia among women, this critique located its cause in the oppression of women by men, particularly as expressed in the premium placed by men on thinness for women. According to Orbach, women's resulting conscious quest for thinness is subverted and betrayed by their unconscious desire for fatness and fear of thinness. On the face of it, there are problems with this explanation: By most criteria, Orbach's American women in 1978 would seem to have been less oppressed than their counterparts of half a century before in Moscow and Berlin. If oppression of women is a cause of bulimia, bulimia should have decreased in prevalence, not increased. Of course, such historical parallels have their limitations. Was the oppression of women that has been considered by feminist writers as a critical element in bulimia today focused to the same extent on pressures for thinness at that time? It may have been; this was, after all, the age of the flapper. But it will take good social history, which is now lacking, to trace the shifts in the ideal of female beauty during this period. The argument from psychodynamics is even less convincing. Wulff's careful analyses found neither of the unconscious motivations that Orbach postulated as etiological in bulimia—the drive for fatness or the fear of thinness.

Wulff's descriptions of bulimic behaviors are likely to prove more enduring than his psychodynamics. They have already made it clear that bulimia is not an exclusively modern disorder. This translation will have served its purpose if it provides investigators with tools for further understanding of this disorder.

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# Toward a Clinical Model of Psychotherapy for Depression, II: An Integrative and Selective Treatment Approach

T. Byram Karasu, M.D.

*This is the second in a two-part series on psychotherapy for depression. Considering depression as a spectrum phenomenon, the author goes beyond manual-based diagnosis to suggest criteria for the use of psychodynamic, cognitive, or interpersonal psychotherapy, with or without pharmacotherapy. He proposes a clinical model that is both integrative and selective and recommends shifting and sharing different therapeutic perspectives in tailoring treatment to the depressed individual.*

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Recent years have witnessed the increasing application of psychotherapy to the treatment of depression, alone or in combination with pharmacotherapy (1–3). Despite numerous conceptual and methodological problems in research and practice involving combined treatment (4–7), clinicians have continued to use and refine new pharmacologic agents and innovative forms of psychotherapy. The latter now include a range of cognitive (2), interpersonal (3), and psychodynamic (1, 8, 9) approaches. As in the larger field of psychiatry, however, there are few models for shifting and sharing therapeutic perspectives (4, 10).

In an initial exploration of this subject, which appeared in the last issue of the *Journal*, three major types of psychological treatment of depression—psychodynamic, cognitive, and interpersonal—were schematically delineated in terms of their respective theoretical constructs, goals, change agents, and techniques; these dimensions were then used to elucidate the assets and limitations of each approach. In this companion article, the three major psychological approaches to depressive disorders are examined further, in terms of both their respective relationships with pharmacotherapy and their application separately or together. These two articles outline both the integration and differentiation of psychotherapeutic approaches to depression and the prospects for ultimate development of a model for clinical practice.

## DEPRESSION AS A SPECTRUM PHENOMENON

Depression spans the entire spectrum of pathology and health. It is manifested in an assortment of psychiatric disorders, which can be psychotic, neurotic, or characterological and can range in presentation from florid, biphasic mood shifts (11) to chronic mild malaise (12) or even masked symptoms that are disguised as behavioral disturbances (13). Depression is also a concomitant of abnormal and normal bereavement and of everyday oscillations of emotion.

Moreover, depressive episodes appear during all stages of the life cycle—as the "anaclitic" depression experienced by hospitalized infants in reaction to early maternal separation (14), as suicide and other behavioral expressions of underlying depression in adolescence (15), as a common concomitant of midlife (16), and as the progressive physiological deterioration that increasingly accentuates, but also sometimes conceals, functional depressive disorders in the aged (17). Each is associated with an advance from one major developmental phase to another, which inherently constitutes a psychological loss of past objects, experiences, and/or possibilities. This may in part account for the recent finding that age does not alter the basic phenomena of major depression, even though it differentially modifies the symptom profile in developmentally different populations. The core symptoms that remain unchanged with age are depressed mood, diminished ability to concentrate, sleep disturbance, and suicidal ideation (18).

In light of its ubiquity, depression has recently been classified into three global categories: normal emotion, symptom, and psychiatric disorder (19). At one end of the spectrum, depressed feelings or passing sadness may be regarded as a natural part of everyone's experience, as an adaptive response to everyday disappointments or as a universal reaction to the ontologic condition of all human existence in face of man's mortality (20). While some existential crises can precipitate a severe depression, most normal affective fluctuations are relatively benign, transient, appropriate to the situation, and reversible. At the other end of the spec-

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trum is illness, the disorders involving "a prolonged emotion that colors the whole psychic life" (*DSM-III-R*, p. 213).

Studies of the similarities and differences between nonclinical depression and mourning have confirmed the resemblance between normal depression and uncomplicated bereavement (21). Beyond this, psychiatric depression has been succinctly defined as "a morbid sadness, dejection or melancholy" and is distinguished from nonmorbid "grief, which is realistic and proportionate to what has been lost" (22, pp. 28). This overriding distinction, whose theoretic roots are found in Freud's classic "Mourning and Melancholia" (23), has both diagnostic and therapeutic implications. Pathological depression is both manifested and subjectively experienced as distinctly different from ordinary sadness (24) or a reaction to the real loss of a love object; it is frequently considered the consequence not of actual loss but of fantasized, excessive expectations that are not—indeed, by their very nature cannot be— fulfilled. Although they differ in duration and intensity, melancholia and mourning are both characterized by painful dejection, cessation of interest or pleasure in the outside world, inhibition of activity or motivation, diminution of the capacity to love, physical vegetative signs (such as reduced appetite or sleep disturbance), and even loss of the will to live or the active wish to die. However, what appears to significantly separate the two phenomena is the fundamental low self-regard in melancholia, which accounts for the profound self-denigration and self-reproach that pervades the overall picture.

Other boundary problems relate to not only such fundamental distinctions as those between normal and morbid affective states, but also the differences between depression and anxiety, between affective and personality disorders, and between schizophrenia and affective psychoses (25). Other definitions also highlight the blurred boundaries in descriptions of depression. For example, depressed "affect" usually refers to transitory fluctuations in feelings, whereas depressed "mood" is frequently descriptive of more enduring emotional states (19). Such unresolved terminology is reflected in APA's *Diagnostic and Statistical Manual of Mental Disorders*, the first standardized diagnostic system to devote a separate category to affective disorders; the generic term "Affective Disorders" was changed to "Mood Disorders" when the manual was revised.

The clinical classification and diagnosis of depression is as yet unresolved (26). It has been a matter of concern and controversy since Kraepelin's pioneering designation of "manic-depressive insanity" nearly a century ago (27), which split major mental disorders of intense affect (either depression or elation) from those marked by the absence of affect, i.e., "dementia praecox" (later renamed "schizophrenia" by Bleuler [28]). Subsequent nosological systems (e.g., autonomous/reactive, endogenous/exogenous, bipolar/unipolar, psychotic/neurotic, primary/secondary, major/minor) have since reflected attempts to extend the affective realm to less severe forms of depression, often broadly differentiating chronic conditions (largely independent of the impact of external events) from situational varieties (related to acute or subacute environmental circumstances). In *DSM-III-R*, "Major Depression" is distinguished from "Dysthymia (or Depressive Neurosis)."

Even today there is still a tendency to dichotomize depressive disorder (29), but we do not yet know whether major depression and dysthymia are truly separate types of illness or exist on a clinical continuum. This question is an expression of the longstanding Kraepelinian/Meyerian dichotomy (binarian) versus continuity (unitarian) controversy (25). Its current status is reflected in a recent conclusion by Andreasen et al.: "Two different components are important in the classification of depression: severity and type of symptoms. The difference between subtypes is probably both qualitative and quantitative, both continuous and categorical. Although this conclusion is complex and paradoxical, it does reflect the reality of clinical practice" (30).

### *Implications for Treatment*

The selection of therapy for an individual patient has typically been insufficient because the clinician bases the choice on 1) his own preferred modality and partisan conceptual position, irrespective of diagnosis, or 2) standardized diagnosis only, to the exclusion of other relevant variables. Both tendencies have begun to be subjected to criticism and reevaluation. Failure to recognize the range of treatments available and the possibility that another therapy may be more suitable than one's own has become a common theme in contemporary psychiatry (4, 10, 31–33). The tendency to address diagnosis only is the result of underappreciation of the spectrum of individual symptoms and patient profiles (34, 35).

The necessity for continual evaluation of standardized criteria for melancholia was pointed out by the originators of the concept themselves (28). In a recent reassessment of the unipolar-bipolar dichotomy, for example, it was proposed that the classification of depression incorporate such nonsymptom considerations as family history, temperament, abruptness of onset, periodicity and seasonality, and response to pharmacotherapy (36). Skodol and I (35) have presented the clinical profiles of three very different patients with dysthymic disorder who were nonetheless identical across all five *DSM-III* axes, and we suggested that there is a need for additional criteria for selection of treatment—e.g., goals of therapy, nature of explicit or implicit contract drawn, anticipated therapeutic relationship and its complications—to make it more individualized.

In sum, the present concept of depression as a spectrum of disorders is based on the complexity of definition and diagnosis and the increasing recognition that affective/mood disorders have many forms, according to their somatic, psychomotor, emotional, cognitive, and characterological features (25). Such a spectrum requires a flexible model of treatment in which particular aspects may be selected and/or integrated.

## PSYCHOTHERAPY AND PHARMACOTHERAPY: THREE APPROACHES

Conceptual or clinical resistance to pharmacotherapy by psychotherapists (and the resistance to psychotherapy by pharmacotherapists) has a long history and is a legacy of the post-Cartesian mind-body dichotomy that has always been at the core of modern medicine (37). The beginnings of an integrative model of psychotherapy and pharmacotherapy have appeared only recently. Affective disorders appear to be the most promising diagnoses with which to assess the additive effects of the two modalities combined (4). Each of the three major psychotherapeutic approaches to depression—psychodynamic, cognitive, and interpersonal—has its own strategies for using pharmacotherapy, which are based on its history and theoretical orientation toward conjoint treatment with medication.

### *Psychodynamic Therapy Plus Pharmacotherapy*

Freud (38) anticipated the potential value of pharmacotherapy when he wrote, "The future may teach us to exercise a direct influence, by means of particular chemical substances . . . . It may be that there are other still undreamt of possibilities of therapy." Nonetheless, the fundamental clinical posture of psychoanalytic treatment has been based on the Freudian premise that symptoms of psychopathology (e.g., anxiety) are the patient's motivation for change and sustained analytic work; reduction of symptoms by somatic means could thus destroy or reduce a crucial motivational source. Apart from this legacy (which may not be as applicable to depressed patients as it had been to anxious ones), psychoanalytic psychotherapists have traditionally resisted administration of pills because the tenets of classical technique inherently disparage methods that do not provoke insight, i.e., any form of external manipulation (39). The introduction of drugs has thus long been construed as an artifact that can confound the therapeutic transference (40).

Despite gradual modification of this view over the years (41), it is still believed that the major risk of administering pharmacologic agents during psychodynamic treatment is that the patient will use them as a crutch or substitute for introspection instead of relying on self-exploration (8). Luborsky (8) pointed out that psychodynamic progress may be impeded if the patient 1) considers taking medication an indication that he is giving up self-control and autonomy, 2) regards the recommendation to take pills as a sign that psychotherapy has failed, or 3) unrealistically views the therapist as an omnipotent figure because he administered the magical medication. (Although this does of course occur, to a greater or lesser degree, in any treatment, depressive patients are particularly vulnerable to overendowing therapists and further diminishing their own self-esteem.) Other potential pharmacologic problems during expressive therapy have also been noted, such as the danger of misinterpreting drug side effects as psychological phenomena or the therapist's defensive resorting to drug administration at difficult points in exploratory work (42).

Although the combination of antidepressants and psychodynamic psychotherapy was rarely applied in the past, modern practice is much more flexible. The predominant psychodynamic stances and strategies regarding adjunctive treatment with pharmacotherapy include general avoidance of its use unless necessitated by an acute, life-threatening situation and, more recently, judicious titrating of pharmacologic agents, especially when somatic symptoms or vegetative signs are pronounced. When drugs are prescribed, their implications and personal meanings are to be explored and interpreted with the patient, as with any other events that are consciously or unconsciously brought into the psychodynamic treatment.

### *Cognitive Therapy Plus Pharmacotherapy*

Overall, research results indicate cognitive therapy alone is effective with a substantial range of clinically depressed inpatients and outpatients and with nonpatients (college students with subclinical depression); the effects are equal to or greater than those of pharmacotherapy and are comparable to the effects of combined treatment (43–45). The results have been accompanied by recommendations for using pharmacotherapy in conjunction with cognitive therapy (2), since depression is heterogeneous and not all depressed patients respond to cognitive therapy alone.

Indications for combining it with pharmacotherapy include inadequate response to cognitive therapy, presence of severe somatic symptoms, impaired concentration and marked psychomotor difficulty, severe depression, history of mania, chronic maladaptive functioning with intermittent depression, evidence that a first-degree relative has responded to antidepressants, and ironically, poor compliance with a medical regimen. In addition, for some patients who do not seem to be responding to cognitive therapy, the conjoint application of antidepressants appears to break the impasse in therapy almost immediately (2).

Cognitive therapy methods specifically designed to increase adherence to medication regimens include written records of side effects and telephone calls to the patient to elicit and correct negative cognitions about medication. Cognitions that have been found to contribute to poor adherence to prescribed medication regimens fall into three categories: before medication (e.g., It's addicting; It's a sign of weakness to take it), during medication (e.g., I should feel good immediately), and general, which involve the depression itself and undermine the patient's willingness to take any

**TABLE 1. Approach to Pharmacotherapy of Three Psychotherapies for Depression**

| Feature of Combined Treatment | Psychodynamic Therapy | Cognitive Therapy | Interpersonal Therapy |
|---|---|---|---|
| Basic stance | Medication is avoided except in life-threatening situation, used judiciously for severe vegetative signs | Pharmacotherapy and cognitive therapy alone are in ongoing competition, but drugs are used in case of poor response to cognitive therapy and for breaking psychotherapeutic impasses in severe depression when symptomatic relief is required | Interpersonal therapy and pharmacotherapy are considered having different effects and response timetables (early drug effects on vegetative symptoms, later psychotherapy effects on suicidal ideation, work, and interests) |
| Techniques | Personal (unconscious and/or conscious) meanings are explored and interpreted within therapy session | Information and rationale for use is provided; special tasks are assigned to increase adherence, e.g., postsession homework (lists of side effects); phone contact with therapist is encouraged | Information and rationale for use is provided, in line with medical model; time is set aside in each session to discuss pharmacological issues |

medication (e.g., I am not ill; I am so ill that no treatment will help).

### *Interpersonal Therapy Plus Pharmacotherapy*

Perhaps more than any other psychotherapeutic modality, interpersonal therapy has been shown to be effective in neurotic and acute depression when combined with drug treatment. In the major studies in this area (46–53), each modality had independent effects, as contrasted to synergistic effects, on different aspects of depressive illness. Pharmacotherapy improved sleep and other vegetative symptoms, whereas interpersonal therapy altered such psychological symptoms as apathy and hopelessness. At 1-year follow-up, combined treatment again proved superior to either alone. In addition, different response latencies were observed: drug effects occurred early in treatment, often within the first week, whereas psychotherapy effects occurred later (47).

Klerman et al. described the combination of interpersonal therapy and pharmacotherapy in depression as a selective but accepted aspect of interpersonal therapy (3). They contended that generally the problems of combined psychotherapy and pharmacotherapy treatment are more attitudinal than real; that is, they do not lie in understanding (or misunderstanding) the pharmacology of drugs or specific problems of treatment but, instead, involve patient and/or therapist views reflecting either larger social values about medication or individual feelings about its use. Rounsaville et al. (51), using clinical data from another study (50), expressly disconfirmed six major hypotheses regarding negative aspects of the psychotherapy-pharmacotherapy interaction.

In earlier research (52) it was found that higher scores on a neuroticism scale were correlated with chronic poor response to one or both treatments up to 4 years after the acute episode. In examining diagnostic subtypes of depression as predictors of differential response to interpersonal therapy and/or drug treatment, Prusoff et al. (53) found that both nonendogenous and endogenous depression responded to combined treatment, the latter did not respond to interpersonal therapy alone, and the former responded to either alone, suggesting that it may be unnecessary to use combined treatment for situational depression.

Klerman et al.'s technical suggestions included giving the patient a preliminary explanation of the rationale for each intervention. During treatment itself they advocated setting aside a specific time, usually at the beginning of each session, to discuss pharmacotherapy therapy issues (e.g., side effects). Another major technical issue for interpersonal therapists is whether there will be one or two therapists for combined treatment; cooperation between psychotherapist and pharmacotherapist is needed when treatment is split.

Table 1 compares the three types of psychotherapy for depression with regard to their respective clinical stances and specific techniques.

## PSYCHOTHERAPY AND PHARMACOTHERAPY: A SELECTIVE AND INTEGRATIVE APPROACH

Although controlled efficacy studies suggest that over 60% of depressed patients improve with common tricyclic drugs (54), the other side of the coin is that nearly 40% do not. Other real constraints of pharmacotherapy in affective illness are the relatively high relapse rate of depressed patients treated with medication (nearly one-half in the year immediately after termination of treatment) and the failure to prevent suicide with antidepressant drug treatment, even after having averted a suicidal crisis (55). From the drug-responsive group may also be subtracted those who show significant side effects (56).

These outcomes can occur with or without the adverse psychological impact of irrational fears or myths about medication (41), which can themselves confound the pharmacologic response. For example, a variety of undesirable psychological concomitants of pharmacotherapy have been cited in the treatment literature, including fear of functioning without external aids and loss of the patient's sense of autonomy as chemicals become a crutch and discourage other, self-initiated therapeutic efforts (57, 58). This possibility is particularly salient with depressed patients, whose reliance on chemotherapy may unwittingly undermine their easily diminished egos and deplete already limited inner resources for coping with depression (2). Still other depressed patients, albeit potentially responsive, may unconsciously or consciously reject medication for subjective (personal, religious, cultural) reasons. In fact, although there are many explanations for nonresponse to drugs, noncompliance with the medical regimen is an often neglected contributor (59); surveys indicate 25% to 50% of those treated for affective illness fail to take their medication as prescribed, reducing or discontinuing its use (60).

On the other hand, however, many patients lack access to psychotherapeutic intervention, and unlike anxiety, depression inherently retards psychomotor energy and motivation for change. In addition, marked resistance at any point during the therapeutic interaction (61) can be exacerbated by the depressed patient's vulnerability to narcissistic injury and by consequent countertherapeutic interpersonal maneuvers to compensate for object loss within the therapist-patient relationship.

These factors illustrate the complementary roles of drugs and psychotherapy; drugs can facilitate a patient's receptivity to psychological intervention by controlling episodes of irritability or apathy, which produce impasses in the interaction between patient and therapist, while psychotherapy may be used for increasing compliance with medication regimens. In fact, specific techniques for drug compliance have been directly incorporated into both cognitive and interpersonal therapy for depressed patients (2, 3). The extension of psychotherapeutic approaches to the patient's spouse or family can also help neutralize the negative influence of family members who otherwise sabotage efforts to adhere to a medication schedule. A major role of psychotherapy may thus be to enhance the response to chemotherapy, by inducing patients to remain in treatment for longer periods, or to provide alternative long-term care for those who do not obtain full prophylaxis or remission from antidepressant medication.

The following clinical model is based on the finding that psychotherapy is increasingly being shown to be effective in the treatment of major depression, alone or in combination with pharmacotherapy (4, 5, 62, 63), and it begins where my earlier combined treatment model for depression left off (4). The prior model was based on the finding that the two treatments together are superior to either intervention by itself: 1) the two modalities have different effects—drugs primarily affect symptom formation and affective distress, whereas psychotherapy more directly influences interpersonal relations and social adjustment, 2) the two are activated and sustained at different times—drugs may take effect sooner and last for shorter periods, whereas psychotherapy results may not reveal themselves until later but can last longer, and 3) they may work best with different diagnoses and subtypes—drugs with time-limited and autonomous state disorders, psychotherapy with more enduring trait disorders (4). In brief, although research on combined treatment has special problems, it seems to indicate that the two modalities are independent and complementary in terms of active ingredients, mechanisms of change, and latency of response (6, 7, 43, 47, 49, 64).

In my earlier model of combined therapy for affective disorders (4), pharmacotherapy was considered the better treatment for mania and major, endogenous depression, whereas psychotherapy was thought to be preferable for minor, reactive, or nonendogenous disorders. However, the diagnostic changes reflected in *DSM-III* in part mirror the new thinking in clinical practice that pharmacotherapy need not be limited to the most severe types of affective disorder (65) and, the converse, that psychotherapy need no longer be relegated to mild forms of depression only (66). Table 2 presents a model of combined psychotherapy-pharmacotherapy that goes beyond the diagnostic rubric in two ways: to the spectrum of signs and symptoms of affective disorders and to clinical variables other than the standard diagnostic boundaries. The constraints of the model must also be noted: these variables are not intended to be all-inclusive and have not been subjected to rigorous research and clinical trials. Moreover, the division of variables between pharmacotherapy and psychotherapy is not meant to imply they are categorical or mutually exclusive but, rather, provides a framework for their selective application within an additive treatment model.

This clinical model emerges out of, and therefore does not negate, the most updated standardized diagnostic guidelines for depression; it breaks diagnosis down to quantitative and qualitative variables that may each respond to either pharmacotherapy or psychotherapy. Major depression is initially broken down into the nine symptom-related criteria designated in *DSM-III-R* (see table 2).

This model suggests that the symptoms of depression have many dimensions: physiological (hypersomnolence, weight loss, somatic disorders, psychomotor retardation), affective (depressed mood, guilt, repressed anger, anxiety), cognitive (negative, pessimistic perceptions and ruminations), interpersonal (social withdrawal, increased helplessness), and behavioral (reduced activities, increased dependency, self-destructive acts) (3). Some of these manifestations are better treated with pharmacotherapy, others with psychotherapy. For example, while psychotic thinking, especially persecutory or nihilistic delusions and auditory hallucinations, can be appropriately treated with medication, persistent irrational beliefs that reflect negative distortion or exaggeration but not psychosis can be effectively treated with psychotherapy. Such differen-

**TABLE 2. Indications for Psychotherapy and Pharmacotherapy in the Treatment of Depression**

| | Indication for Treatment[a] | |
|---|---|---|
| Variable | Pharmacotherapy | Psychotherapy |
| *DSM-III-R* symptom criteria for major depression | | |
| Depressed mood | Marked vegetative signs; extreme or uncontrolled mood | Mild to moderate situational or characterological depressed mood |
| Diminished interest or pleasure | Anhedonia; loss of libido; impaired sexual function or performance | Apathy, decreased enjoyment; diminished sexual desire or gratification |
| Weight loss or gain | Significant weight loss | Insignificant weight gain |
| Insomnia or hypersomnia | Early morning wakening | Oversleeping, morbid dreams or nightmares |
| Psychomotor agitation | Hyperactivity or motor retardation | Restlessness or feelings of being slowed down |
| Fatigue or loss of energy (anergia) | Depressive stupor | Lack of motivation or will |
| Feelings of worthlessness or excessive guilt | Nihilistic or self-deprecatory delusions, self-berating auditory hallucinations | Low self-esteem, inappropriate guilt feelings, self-reproach |
| Diminished ability to think or concentrate, indecisiveness | Loss of control over thinking, obsessive rumination, inability to focus or act | Distractibility, sluggish thinking or decision making; negative cognitions |
| Recurrent thoughts of death or suicide | Acute, episodic, and uncontrolled suicidal acts or plans[b] | Chronic feelings of hopelessness or helplessness[c] |
| Associated features | Panic (anxiety) attacks or phobias; persecutory delusions; pseudodementia; physical symptoms or somatic delusions | Social withdrawal or fears of rejection or failure; psychosomatic complaints or hypochondriasis |
| Family history | Genetic loading (bipolar or unipolar illness) | No genetic loading (dysthymia) |
| Predisposing factors | Other mental disorders, e.g., schizophrenia, alcoholism, anorexia nervosa | Psychosocial stressors, e.g., loss of significant other, change in status or role |
| Personality disorders | Borderline, histrionic, obsessive-compulsive | Dependent, inadequate, masochistic |

[a] These are not mutually exclusive categories.
[b] Hospitalization may be required.
[c] Medication may also be useful.

tial treatment also applies to observable psychomotor agitation or retardation versus feelings of restlessness or being slowed down and early morning wakening versus morbid dreams or nightmares.

These symptoms, signs, and associated features may not suffice, either quantitatively or qualitatively, as clinical criteria in developing a combined psychotherapy-pharmacotherapy model. The contributions of a variety of other relevant variables, e.g., family history, nature of onset, predisposing factors, and personality type, pose the need for vigorous research and eventually a more comprehensive joint treatment model of depression that takes diverse genetic (67), environmental (68), physiological (69), and biochemical (70, 71) factors into account (72).

## SELECTING PSYCHOTHERAPY FOR INDIVIDUALIZED TREATMENT

In addition to the aforementioned variables are the therapeutic vicissitudes of the treatments themselves, the patients for whom they are best suited, their processes, and their goals. Not only may patients be differentially amenable to different treatment modalities, but different treatments may produce different effects.

Table 3 sets the stage for using the three models of the treatment of depression as both unique and potentially complementary. It first lists some "nonselective" variables—hyperphagia, hypersomnolence, leaden feeling, sensitivity to rejection, feelings of inadequacy, diminished self-esteem and interest, anergia, undue guilt, difficulty in concentration or decision making, recurrent thoughts of death, unrealistic ego ideals and expectations, helplessness, hopelessness, and deficits in interpersonal relations—that may be shared, to greater or lesser degrees, by all depressed patients and may be helped by any of the three psychotherapies or by other approaches not discussed here. It then lists an additional array of "selective" variables that may call for or contraindicate each of the three specific psychotherapeutic approaches. These variables include not only *DSM-III-R* diagnostic features and other individual variables, but the goals and overall characteristics of each approach—in short, a blend of patient and technical psychotherapeutic factors that can be used in selecting one or more modalities for individualized treatment.

The goals of the psychodynamic approach are insight, conflict resolution, and personality modification, and its methods are examination of the intrapsychic structure of illness, in-depth exploration, and longitudinal, developmental orientation to the present in relation to the past. It may be particularly suitable for treating chronic, pervasive low self-esteem and dejection and excessive feelings of guilt, especially in pa-

**TABLE 3. Nonselective and Selective Patient Variables for Psychotherapy of Depression**

| | Selective Patient Variables | | |
|---|---|---|---|
| Nonselective Patient Variables | Psychodynamic Therapy | Cognitive Therapy | Interpersonal Therapy |
| Feelings of hopelessness and helplessness<br>Apathy, decreased enjoyment, diminished desire or gratification<br>Too high ego ideals and expectations<br>Oversleeping, morbid dreams or nightmares<br>Feelings of restlessness or being slowed down<br>Lack of motivation or will<br>Low self-esteem, inappropriate or excessive guilt and self-reproach<br>Distractibility, sluggish thinking or decision making<br>Wish or intention to be dead<br>Social withdrawal, fear of rejection or failure<br>Psychosomatic complaints, hypochondriasis | Chronic sense of emptiness and underestimation of self-worth<br>Loss or long separation in childhood<br>Conflicts in past relationships (e.g., with parent, sexual partner)<br>Capacity for insight<br>Ability to modulate regression<br>Access to dreams and fantasy<br>Little need for direction and guidance<br>Stable environment | Obvious distorted thoughts about self, world, and future<br>Pragmatic (logical) thinking<br>Real inadequacies (including poor response to other psychotherapies)<br>Moderate to high need for direction and guidance<br>Responsiveness to behavioral training and self-help (high degree of self-control) | Recent, focused dispute with spouse or significant other<br>Social or communication problems<br>Recent role transition or life change<br>Abnormal grief reaction<br>Modest to moderate need for direction and guidance<br>Responsiveness to environmental manipulation (available support network) |

tients with severe real losses, extended separation in childhood, or long-standing unresolved conflicts related to attachment and loss in early relationships. At the same time, the psychodynamic approach generally requires that patients have a capacity for trust, good object relations, and a relatively stable environment and social support system. They must also be psychologically minded, have the capacity for insight and self-understanding, and have the ego strength to modulate regression when frustrated by a relatively neutral therapist within a transferential relationship. When the therapist is more direct or active (in short-term psychodynamic approaches), the patient must especially be able to deal with the anxiety resulting from confrontation of his defenses, early presentation of his conflicts, or immediate focus on the transference. These requisites, of course, are moderated by the duration, flexibility, and focus of the particular psychodynamic treatment and whether an open-ended (1), short-term (8, 9, 73, 74), or set time frame (75) is used.

Whereas the psychodynamic approach primarily focuses on the internal mechanisms of the illness, individual memory, and childhood antecedents of current object relations and achieves its goals through confrontation or interpretation of defenses and the patient's gradual uncovering of unconscious motivations, the interpersonal approach mainly addresses the social context or consequences of the illness, focuses on current environmental stressors and life events, emphasizes the recognition of assets, helps the patient correct misinformation, and provides direct advice on alternatives. It may be especially helpful for patients with recent, focused interpersonal disputes or communication problems, for those who are acutely distressed over a major role transition or marital discord, and those who have experienced real losses. Gotlib and Asarnow (76) found that depressed subjects performed significantly more poorly on an interpersonal problem-solving task than on an impersonal task. This was interpreted as evidence for the specificity of an interpersonal problem-solving deficit in depressed individuals. Discernible interpersonal problems or social deficits could also be subjected to environmental manipulation (e.g., a marital partner brought into treatment). Interpersonal therapy's communication/environmental methods (i.e., clarification and management of maladaptive relationships and negotiation of new ones through communication and social skills training) may be especially useful with depressed patients who need more active engagement with the therapist. These patients may also rely more on outside relations for self-esteem and productive functioning than patients who are appropriate for a psychodynamic approach.

The cognitive approach would be most suited to patients whose negative distortions of themselves, the world, and/or the future are readily apparent. In validating its unique effects, for example, Rush et al. (77) found that cognitive therapy had a more pervasive and significant impact on self-concept by the end of treatment than did amitriptyline, and it also resulted in quicker reduction of hopelessness. These findings suggest that this type of approach specifically improves patients' views of themselves. Patients with greater cognitive distortions responded better to cognitive therapy than did patients with less negative thinking.

The methods of cognitive/behavioral therapy do not require that the recipients of cognitive therapy be introspective. Rather, they can be pragmatic and therefore capable and responsive to logical thinking that does not demand a capacity for insight. They may also be more in need of strong guidance and direction for developing new patterns of thought. Such patients have been shown to have a high capacity for self-control (78), so they may especially benefit from behavioral exercises and home practice, which are an integral part of cognitive therapy.

## CONCLUSIONS

The variation of depression in terms of etiology, manifestations, and response to treatment is well documented (11, 25, 79). Moreover, no single therapy is uniformly successful for all the concomitants of the depressive disorder (46, 47). For instance, biological variables may override psychological ones, or the reverse. In addition to determining whether treatment should consist of drugs combined with psychotherapy or of psychotherapy alone, examination of the three psychotherapies lends itself to a more discriminatory use of each, as indicated in part I of this series.

Psychotherapy may be effective alone or combined with pharmacotherapy for a variety of patients and variables pertaining to both the illness itself and to change mechanisms and timing of treatment effects (6, 7). In some instances, a distorted viewpoint that has been targeted for change is isolated, recorded, monitored, logically analyzed, and ultimately brought under the patient's control with the teaching and support of the therapist. This process brings about salutary change, overt symptom relief, and/or prophylactic effects that endure beyond the acute episode and can be applied to subsequent recurrences. In other cases, the sociocultural context may be crucial because of specific environmental stressors. In yet other cases, where the effects of these approaches are at best temporary and changes in depressogenic thinking or environmental management do not alter chronic conflicts or profound fears of loss of love, a deeper approach may be necessary to tap the unconscious memories or schemata beneath the surface, thereby requiring greater efforts toward structural modification.

Psychotherapy may thus be used not only by default, that is, to increase compliance with medication or as an alternative for patients who cannot or will not respond to pharmacotherapy, but in itself as an independent intervention. Cognitive therapy can be used to change depressogenic attitudes and ingrained thinking patterns. Interpersonal therapy emphasizes teaching specific communication and social skills to counteract deficits or disputes involving a spouse or significant others in one's personal or work life; these deficits can be causes or consequences of depression. Psychodynamic therapy addresses the individual's intrapsychic conflictual personality structure so that the underlying demoralization of the damaged self, which dominates the clinical core of depression, can be understood and thus altered.

Although these three psychotherapeutic approaches represent different conceptualizations of depression as a disorder and have direct implications for therapeutic processes and change agents, even in the operationalized, research-oriented manuals they are not represented as categorical in practice (2, 3, 8, 9). They have the common elements shared by all psychotherapies (e.g., benign human relationship) (80, 81), and they may complement each other in their basic modus operandi and in fundamental change agents, i.e., cognitive mastery, affective experiencing, and behavioral regulation (31, 33). Moreover, the controversy of nonspecificity versus specificity of therapeutic effects (33) might be resolved by acknowledging that the former sets the stage for the latter. Common elements (empathy, positive regard) are applied to establish contact with the patient (therapeutic alliance), while specific techniques can be applied separately or together to bring about affective, cognitive, and/or behavioral changes. Simultaneously, each modality may be highly specific—applicable to certain subgroups of depressed individuals. The prototypical depressed patient in interpersonal therapy has recent, focused disputes with a spouse or significant other, cognitive therapy patients are characterized by habitual faulty thinking, and dynamic therapy is suited for patients with chronic conflict and lack of self-esteem. These and other psychotherapeutic approaches must also interact with pharmacological treatment, which has its own variations in efficacy and specificity (5–7).

Future directions for research thus entail increasing refinement of depressive subtypes, both diagnostically and therapeutically. In terms of diagnosis, we must identify depressed patients' particular assortment of symptoms, severity and level of functional impairment (82), and their accompanying biological, psychological, and social characteristics. In terms of therapy, we must determine doses and durations of treatment, identify effective combinations, and determine sequences of response. However, neither search need preclude addressing what all depressed patients or all therapies for depression hold in common. The proposed approach to clinical practice is therefore both integrative and selective. The integrative aspect pertains to collective qualities of all patients and to shared aspects of different therapeutic approaches, in whole or in part. The selective aspect refers to special features of such patients and therapies—what they can contribute together and separately.

Recognizing depression as a spectrum phenomenon is the first step. The diagnosis of unipolar depression, for example, may not define a population narrowly enough to permit proper patient assessment or determination of effective techniques for these particular patients. The diagnostic task of the future is thus to identify biopsychosocial variables that go beyond symptoms alone in delineating the individual clinical disposition. There is also a parallel need for recognition of increasing diversity in the treatment armamentarium for depressive disorders, both within the psychotherapeutic domain (e.g., cognitive, interpersonal, psychodynamic, and other therapies) and outside its boundaries (e.g., pharmacotherapy). Achievement of maximal therapeutic efficacy necessitates not simply knowledge of one's own school or theoretical orientation but appreciation of what other modalities and techniques have to offer (82, 83). In the best of all worlds, psychiatrists may well master only one modality, with which they identify and maintain allegiance, yet be well versed in the wide spectrum of strategies available. Moreover, both psychiatrists and primary care physicians can bear in mind an unanticipated, newly published finding from the National Institute of Mental Health Treatment of Depression Collaborative Research Program (82): the value in the clinical management of depressed patients of an initial supportive approach (sympathetic attention and encouragement beyond pill placebo), with or without pharmacotherapy—before specific treatment begins (84).

In sum, instead of focusing on which single school of therapy is effective for the large universe of unipolar depression, ideally one should take a highly individualized approach to meet each depressed individual's needs, using a broad-based but selective shifting and sharing of therapeutic perspectives. Realization of this effort, however, may be reminiscent of sentiments expressed over three centuries ago in *Anatomy of Melancholy*, the first detailed description of depression and its treatment. Its author, English clergyman and scholar Robert Burton, who suffered from chronic depression himself, despairingly suggested that "for this particular disease, him that shall take upon him to cure it . . . will have to be a Magician, a Chemist, a Philosopher, an Astrologer" (85, p. 390). The therapy of depression may no longer be as difficult a task as it was in Burton's day, but as an early portent of the need for an approach to depressive disorders that is both integrative and selective, his multifaceted model still holds.

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# Sequelae of Bereavement Resulting From Suicide

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*Although clinical experience suggests that individuals who have been bereaved as a result of suicide may be especially vulnerable to adverse sequelae, such as unusually severe grief or increased risk of committing suicide themselves, the idea that this type of bereavement is special has received only limited systematic investigation. The authors review the literature on the subject, with special attention to the clinical and research evidence about whether bereavement resulting from suicide is different from bereavement due to other types of death, and make suggestions for further clinical and epidemiological research on this question.*

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The loss of a family member or an intimate friend due to suicide has long been considered an especially stressful life experience. From a public health perspective it is also, unfortunately, not an uncommon experience: more than 30,000 suicides occurred in 1988 (1). More than one-fourth of these suicides were of persons aged 24 or younger who, it may be expected, left at least several surviving family members, including children. Clinical reports have strongly suggested that individuals who have been bereaved because of suicide undergo an especially difficult and distressing form of grief and are also at increased risk for other kinds of adversity following their bereavement (2–4). One of the first clinicians to call attention to this problem suggested that "the person who commits suicide puts his psychological skeleton in the survivor's emotional closet—he sentences the survivor to a complex of negative feelings and, most importantly, to obsessing about the reasons for the suicide death" (2, p. 22). However, despite such clinical impressions, the idea that bereavement due to suicide differs from bereavement due to other types of death does not appear to have been widely accepted. A reflection of this attitude is that research studies on bereavement usually have not even assessed the impact of this type of death. Although several reviews of the subject (5–8) have concluded tentatively that bereavement due to suicide is indeed especially stressful, these reviews have focused primarily on uncontrolled clinical reports, they have not included the full range of research findings that might bear on the issue, and they have varied in their critical attention to the research methodologies of the reported studies.

In this paper we review what is known about bereavement due to suicide compared with bereavement resulting from other kinds of death. We consider 1) whether there is a difference in terms of the grieving process of the bereaved individuals, 2) the social and psychological adjustment of the bereaved after the suicide, 3) their family backgrounds, 4) their mortality rate, particularly in terms of their own risk of suicide, and 5) the attitudes of others in society toward the family members of a person who has committed suicide. Finally, we discuss some methodological problems with the research to date and suggest considerations for further research.

## BEREAVEMENT DUE TO A DEATH OTHER THAN SUICIDE

"Normal" bereavement is marked initially by painful pining and anxiety upon remembering the deceased person, along with sleep disturbance, crying, social withdrawal, difficulty concentrating, and loss of capacity to adopt a new object of love (9–11). Over varying lengths of time, usually measured in months to several years, bereaved persons gradually reengage in their social world. Few of them seek psychiatric help. Although bereavement has sometimes been taken as a paradigm of depression, it rarely leads to major depressive illness and is not regarded as a psychological illness in itself. There is an increase in indicators of morbidity, such as use of medical services and consumption of cigarettes, alcohol, and tranquilizers, but there is no clear evidence for an increase in the incidence of specific medical illnesses. There does appear to be an increase in mortality among certain groups, especially elderly men who do not remarry (6, 12).

Various types of adverse psychological outcomes, or so-called "pathological grief," occur in a substantial number of the bereaved; the exact proportion depends upon how this disorder is defined. These adverse out-

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comes may include a persistant focus on the deceased person, ongoing depression, or chronic illness behavior and may be due to such factors as the nature of the relationship with the deceased individual or the suddenness of the death (13–17).

All of these findings come largely from research on bereaved spouses. By contrast, research on bereavement in children and in the elderly is sparse. Studies of the bereavement responses of children to the loss of a parent (18–20) suggest that such a loss is often a major trauma and may cause behavioral and emotional problems that persist for years. The eventual development of adult psychopathology has been shown to correlate with the quality of home life and personal adaptation subsequent to the loss of a parent during childhood (21).

The response to unnatural types of death has also been only slightly studied, although some reports have suggested that such deaths, including suicide, may lead to specific psychological effects on bereavement (22). There has been one study of bereavement following the murder of a child, sibling, or spouse (23). All of the 15 adult subjects had previously experienced the nonhomicide death of a relative and thus could compare their own two grief experiences. Unanimously they reported persistant fearfulness, anger toward the murderer, and intrusive repetitive images of the murder as they imagined it to have happened. These responses, the subjects felt, were quite distinct from their experiences of grief after the nonhomicide deaths.

Other reports have dealt with reactions to the death of a child from severe burns (24), the death of adult children in traffic accidents (25), and the death of adult children from cancer (26). Each of these reports documented a psychological response appropriate to the particular type of death, such as severe feelings of guilt associated with a child's having been burned, more intense grief and guilt among parents whose children died while driving alone in their own cars, and less intense grief, with more sense of relief, if a child's death from cancer followed a long and debilitating illness. These clinical reports suggest that the type of death may affect the psychology of the grieving process in specific ways.

## THE GRIEVING PROCESS AFTER SUICIDE

Several studies have explored whether the grieving process after suicide has distinctive features. In one study (27), at a time 6–8 months after the suicide of a husband or wife, family members were given a semistructured interview about the effects of the death on their emotions, living situations, health, and coping. The author found that most individuals, upon learning of the suicide, felt shock, disbelief, sadness, guilt, and anger. Over time, more than half experienced crying spells, depression, deep unhappiness or apathy, or persistent anxiety, and several of the bereaved experienced suicidal ideation of their own. The physical health of most of these individuals remained the same.

Subsequent to the initial shock, the bereaved began a prolonged period of searching for an explanation for the tragedy. About half felt that a suicide in the family was a stigma and were unwilling to discuss the event with others, least of all with their children. These individuals experienced less relief and less sadness, but more anger and guilt, than did the other respondents. Few individuals requested help from mental health professionals. In commenting on the number of participants in the study—39 of 82 possible respondents—the author reported that the group which could not be contacted for interviewing contained more black families (only one of seven was interviewed) and more women. The author noted that many of the deceased men had been socially isolated and that many of the surviving family members, such as the spouses, had moved back to their families of origin.

Several aspects of this study are worth noting. One is the reported searching for an explanation for the tragedy, which frequently occurs in the anecdotal literature on bereavement due to suicide but is notably absent from most clinical reports on bereavement due to death under other circumstances. Second, the author's reports about family difficulties and the social isolation of the spouses suggest that family history may contribute in an important way to the aftermath of suicide. Third, the numbers and identities of the respondents raise the possibility that social isolation or the spouses' returning to their families of origin may have affected the recruitment of subjects and caused a selection bias. Finally, a methodological weakness of this study was the absence of any comparison group of families that experienced deaths other than suicides.

Another study (28) examined the impact of suicide versus natural death on 108 elderly bereaved individuals 2 months after the deaths. An interview and five standardized scales were used to assess depression, overall mental health, and psychological distress due to grief. The authors found significant differences on most measures between the bereaved groups and a nonbereaved control group. However, the two bereaved groups differed only in that those whose bereavement was a result of suicide showed a higher degree of anxiety. Because of the low study response rate of 35%, individuals who had refused to participate were recontacted by telephone. They reported that they were coping well with their loss; however, these nonparticipants were older, less educated, and in poorer physical health than the group that participated.

To our knowledge, this has been the only study of elderly persons whose bereavement was due to suicide; its design incorporated comparison groups, statistical controls for intergroup differences, and data on nonparticipants. However, the group that was bereaved because of suicide was younger, was occupationally less skilled, and included more women than the other groups. The nonparticipants, too, differed as a group from the participants. Finally, there were no follow-up data; as the authors pointed out, the bereaved were still in the relatively early stages of grief, when other differences might have been less striking than their acute reactions to the deaths. Thus, the findings of this study are of unclear significance.

The process of grieving after suicide has been portrayed in clinical case reports as having certain common and uniquely disturbing aspects. One is the persistence of frightening and disturbing images of the death, whether that scene was actually witnessed or is imagined (29). One report (30) mentioned the "triple loss" with which the spouse is left to deal: the death itself, the implicit rejection by a loved one who preferred death to ongoing companionship, and disillusionment about a person whom the survivor had admired. A psychiatrist whose wife committed suicide described struggling during the rest of his life to integrate the "existential sequestrum" of his knowledge that his beloved wife chose to end her life (31). Suicidal ideation has been noted to occur in some individuals who are bereaved because of suicide (32).

Although the major focus of this paper is on bereavement due to a suicide in the family, the process of grieving after suicide may also be exemplified by the experiences of other individuals who have an intimate connection with a person who commits suicide. An example of such a connection is a psychotherapeutic relationship. Among staff members and patients in psychiatric treatment settings, the suicide of a patient has been found to produce marked feelings of shock, guilt, and anger (33–37). Some patients have become increasingly fearful about their own suicide potential. Psychotherapists have reported that the suicide of a patient elicited in them shock, grief, and anger, along with guilt and self-questioning about whether they had missed something important that the patient was saying (38–41). With striking unanimity therapists have said that formal and informal consultation with colleagues is one of the most important and helpful actions to take in coping with a patient's suicide.

On the other side of the equation, there have been several reports about patients whose psychiatrists committed suicide (42–44). All of these patients felt shocked, angry, and abandoned. In addition, they experienced demoralization and doubts about their own prospects for being helped, because they perceived the fallibility of their therapists in having committed suicide. The patients seemed to have perceived a double loss: that of the therapist as an individual and that of their faith in therapy itself.

In summary, reports about the grieving process after suicide associate it with certain apparently special experiences, including a sense of shock, a need to search for an explanation, and difficulty in sharing one's feelings about the suicide. Feelings of guilt may be strong and may persist. Such impressions, although based on reports of uncontrolled studies, are consistent, and their face validity is supported by numerous articles in the media and in current literature as well as in professional journals. The single controlled research report (28) failed to show any difference associated with bereavement due to suicide except for a higher degree of anxiety, but the significance of this result is unclear.

## SOCIAL AND PSYCHOLOGICAL ADJUSTMENT AFTER SUICIDE

Three studies have compared social and psychological adjustment after suicide and after other types of death. In one study (45, 46), 20 widows whose husbands had committed suicide were compared, 1–2 years after the deaths, with 20 widows whose husbands had died suddenly under other circumstances. Approximately 25% of the potential subjects could be contacted and consented to participate. There was no difference between groups in terms of overall social adjustment; however, among the widows who had been bereaved as a result of suicide there was significantly more guilt and resentment as well as more social isolation. More than half of the men who had committed suicide had made previous suicide attempts, and 40% of their widows had separated from them before the time of their deaths. It was the author's impression that the widows of the men who had committed suicide had undergone fewer role changes since their spouses died, perhaps because many of these women had withdrawn emotional attachment from the spouse before the suicide and had developed a social life and an identity apart from the spouse. In contrast, the widows whose husbands' deaths were not suicides remained more dependent on the spouse up to the time of death; for them, therefore, the death was more disruptive. The author did not comment about whether marital problems might have contributed to the suicides. The conclusions of this study were weakened by some inconsistencies in the presentation of data and by the low response rate; the latter raises again the issue of potential selection bias.

Another study (47) explored whether individuals who have been bereaved because of suicide tend to isolate themselves socially after the death and, if so, whether this behavior might affect their health over the following year. Questionnaires were sent to 20 widows 1–2 years after their husbands had committed suicide and to 19 widows 1–2 years after their husbands had died in accidents. The widows were asked about their physical health, coping strategies, and the degree to which they discussed the spouse's death with close friends or counselors. Half of the questionnaires were returned; there was no difference in response rate between the widows who had been bereaved because of suicide and the others. While fewer health problems were found among widows who confided in others about their feelings toward the death, there was no difference in frequency of confiding between those who had been bereaved as a result of suicide and the other widows. There were no data about the nonresponders.

A recent study (48) compared 13 widows whose husbands had committed suicide with 13 whose husbands had died in accidents. Potential subjects were contacted by mail and by telephone 4–24 months after the deaths; half of those contacted agreed to participate. At a mean of 15 months after the deaths, the subjects were interviewed and completed questionnaires about the family's response to the death, its functioning, and its support network both before and after the death. Scores on the questionnaires revealed no differences between the groups in their satisfaction with the family's functioning before and after the husband's death, on the degree of life stress experienced, or on psychiatric symptoms. However, the interviews revealed that the widows of men who had committed suicide became more emotionally distant and avoided their families; they also more often concealed the cause of death from other family members. In the suicide group, but not in the accident group, there was an atmosphere of guilt and blaming that involved both the widow and the children; this was due to feelings within the family and to blameful attitudes of other family members. It must be noted, however, that only those who could be reached approximately a year after a death were asked to participate in this study.

In a study of 100 suicides (49), 44 surviving spouses were assessed by means of a semistructured interview on various aspects of their personal, family, and social adjustment 5 years after the deaths. For 10 of the spouses who had died, information was obtained from death certificates, terminal hospital admission charts, and surviving relatives. In addition, the interviewers evaluated outcome by comparing the spouses' situations at the time of the suicides with their situations when they were interviewed. Outcome was rated as better for about half of the spouses and worse for the other half. Better outcome for the bereaved spouses was associated with alcoholism, disturbed personality traits, or previous suicidal behavior on the part of the deceased or with marital separation at any time. The authors thus inferred that the better outcome for some spouses after suicide might have resulted from the removal of the burden of living with a disturbed individual.

All of the studies we have just mentioned concerned social and psychological adjustment after the suicide of a spouse. The impact of a parent's suicide on the psychological and social adjustment of children has been the subject of only one study (50), which drew on the database of the 100 adult suicides mentioned previously. Twenty parents who committed suicide left 36 children who met the study conditions of being older than 2 years of age and of living with the deceased at the time of the suicide. Each surviving parent was interviewed about the child within a few weeks of the death and again 5–7 years later. Information from these interviews, along with school reports, yielded an assessment of the child's overall functioning, school performance, psychological symptoms and treatment, and relationships with the rest of the family. No direct clinical assessment of the children was attempted. A high rate of disruption prevailed in the bereaved children's home lives before the suicide: marital separations had occurred in half of the families, one-third of the parents had at some time been in trouble with the police, and one-third of the children were not living with both parents on the day of the suicide. After the suicide, one-third of the children showed behavior problems, persistent anxiety, aggressive behavior, or signs of withdrawal. At the time of the second interview, half of the children were functioning adequately and half inadequately. Poorer functioning in the children was associated with the parents having had marital separations, trouble with the police, or evidence of personality disturbance before the suicide. Unfortunately, the indirect nature of the assessments of the children in this study limits the types of conclusions that can be drawn, and the use of only two points of assessment, separated by years, omitted data on a large portion of the children's lives.

In summary, the studies on psychological and social adjustment after suicide are weakened by various methodological problems. They do, however, suggest that the suicide of a spouse is often preceded by a marital separation, which may be protective for the spouse who survives. It is unclear whether those who were available and who chose to participate in these studies constituted a self-selected group with greater independence and greater willingness to leave a troubled marital situation. The results of the study of children, while sketchy, suggest that the suicide of a parent may produce severe effects in some children, but the lack of a comparison group and of additional information about development prevents us from determining to what extent the children's problems predated the suicide.

## MORTALITY ASSOCIATED WITH BEREAVEMENT AFTER SUICIDE

The only existing data, to our knowledge, on mortality associated with bereavement after suicide concern the risk of suicide among the survivors. Other potential causes of increased mortality in this group do not appear to have been investigated. One study (51) investigated whether bereavement is a cause of suicide among the widowed. Among other findings, the authors discovered eight suicides among widowed individuals whose spouses had also committed suicide. In contrast, only one suicide occurred among widowed individuals whose spouses had died under other circumstances. This led the authors to conclude that bereavement resulting from suicide is a special risk factor for suicide among the widowed. The statistical basis of their assertion is, however, unclear.

In another epidemiological study that included some data on mortality after suicide (52), 95,647 widowed persons were followed up. During a 1-month period, there were two cases in which the suicide of one spouse was followed by the suicide of the surviving spouse. Unfortunately, the authors did not study the incidence of suicide among the widowed during a period longer than 30 days, nor did they investigate whether the spouse of an individual who commits suicide is at increased risk in general.

Looking at the question retrospectively, one may ask whether individuals who either attempt suicide or commit suicide have histories of exposure to suicide in their family or social backgrounds. Such questions tend to be applied to children and young adults rather than to spouses. In one such study of 12- to 19-year-olds who committed suicide (53), families, friends, and teachers were interviewed about the deceased youngsters. By contacting families immediately after the suicides, the authors achieved an 83% response rate. Compared with a matched control group of nonsuicidal friends, those who committed suicide had been exposed significantly more often to suicide attempts or threats by relatives or friends. The authors concluded that "exposure to suicide or suicidal behavior of relatives and friends appears to be a significant factor in influencing a vulnerable young person to commit suicide." A crucial aspect of this study was that the researchers were able to obtain a high response rate by making immediate contact and, presumably, by winning the trust of the respondents.

In another study (54), a comparison was made between the charts of 243 psychiatric inpatients with family histories of suicide by first- or second-degree relatives and the charts of 5,602 patients without such a family history. Half of those with family histories of suicide had attempted suicide one or more times, compared with one-fourth of the control group. In addition, half of the patients with family histories of suicide received diagnoses of affective disorder, compared with only one-fourth of the patients with no family history of suicide.

Taken together, these studies contribute some evidence that bereavement due to suicide may be associated with an increased risk of premature death due to suicide. Methodological weaknesses of the studies include relatively small effects (especially in the epidemiological data) and retrospective information gathering. In addition, the data do not allow distinctions to be made among the relative contributions of several different factors that might predispose toward suicidal behavior, such as familial affective disease, familial suicidal tendencies, and bereavement itself.

## SOCIAL RESPONSES TO INDIVIDUALS BEREAVED BECAUSE OF SUICIDE

Family members of persons who have committed suicide have often stated in anecdotal reports that they are blamed and shunned by members of the community and by other members of their own families. Social psychologists have sought to assess the reality of these perceptions by giving fake newspaper reports of deaths to volunteer subjects and then asking about their reactions and attitudes toward the bereaved. In one such study (55), the subjects rated the parents of a child reported to have committed suicide as less likable and more to blame for the death than the parents of a child reported to have died from a viral illness. A similar study (56) included accident as one of the alternative hypothetical causes of death; again, the parents were more often blamed for the suicide than for the other deaths.

Finally, there have been two studies of college students who knew a person who had experienced the death of a friend or a relative during the previous 1–3 years (57, 58). In the first study, a structured interview of these students revealed that they found it more difficult to talk with those who had been bereaved because of suicide, and more difficult to express sympathy to the family of a person who had committed suicide, than was the case with individuals who had been bereaved because of accidents or natural deaths. In the second study, the students tended to attribute more blame to those who had been bereaved because of suicide. They also reported that these bereaved individuals had received more mixed messages from others after the suicide.

These reports corroborate the feelings of suicide victims' family members that they are more blamed and avoided than are the relatives of persons who die under other circumstances. This suggests the likelihood of social reinforcement of the self-blame and guilt that already preoccupy the bereaved person.

## DISCUSSION

The data suggest that there are differences between bereavement due to suicide and bereavement due to other types of death. However, these data are far from conclusive.

By comparison with reports about grief in general, reports on grief after suicide emphasize a specific content in the preoccupations of the bereaved: there is first a sense of shock and then a process of searching for the meaning of the tragedy. Being close to such an event appears to have a profound emotional impact. The suicide remains an incomprehensible fact about a loved one. Although such reports are highly consistent in the literature on bereavement due to suicide and have high face validity, it would be important to know whether controlled studies confirm that this kind of emotional impact is distinctively associated with bereavement due to suicide.

Suicide of a family member may also be a risk factor for suicide of the bereaved individual. The fact that some suicidal individuals have a history of exposure to suicide does not prove, of course, that bereavement due to suicide is a risk factor for all such bereaved persons. Nevertheless, this finding of a risk factor has been reported in well-designed studies, and it is consistent with clinical observations. Thus, it is at least a plausible idea and worthy of further investigation.

There may be significance in the numbers and identities of the individuals who could be located for interviews on this subject and who agreed to participate in the studies. It appears that a number of spouses and their children either moved back to their families of origin after the suicide or had separated before the occurrence of the suicide. Whether this happens more frequently among individuals who are bereaved because of suicide than among other groups is a question that is raised by the studies we have mentioned, but it is not answered by the data.

Finally, there is a highly consistent set of findings that social attitudes are more blaming toward individuals who have been bereaved because of suicide. In this sense, these individuals are set apart socially from other bereaved people.

Our review suggests that in the design of future research, it is crucial to avoid the potential selection bias of including only family members who are available after a period of months to years in the area where the suicide occurred. Making contact within a short period after the suicide would reduce the likelihood of missing families that move away. In addition, such rapid contact, if presented as an attempt to be helpful, might maximize the family's willingness to participate; it would also provide a basis for long-term follow-up study. Future research also should include comparison groups of individuals whose bereavement has resulted from deaths that were not suicides and should include repeated assessments of the bereaved over time.

In addition, our review strongly suggests that future studies should include assessments of family history, of the degree of preexisting family disruption, and of the family's socioeconomic situation after the death, since these factors may play a significant role in determining the course of life for bereaved individuals after a suicide in the family. Specific ways in which such factors may have an influence are suggested in a review of epidemiological studies of mortality after bereavement (59). These include 1) homogamous mating of individuals who are vulnerable to stress, to self-destructive behavior, or to suicide itself, 2) a shared social environment of stress or morbidity in the family predating the death, 3) a change in life circumstances after the death that would place the bereaved at risk, such as the absence of financial support or of personal care that had been provided by the deceased, 4) a change in the health practices of the bereaved, such as increased use of alcohol or decreased attention to early evidence of disease, and 5) genetic transmission of factors related to depressive illness, to suicide, or to other potential risks.

We note that our recommendations complement the conclusions of a study by the National Academy of Science's Committee for the Study of Health Consequences of the Stress of Bereavement (6). This study identified the following general problems with current research on the process and outcome of bereavement: limited study of risk factors for adverse consequences of bereavement, too little attention to the impact of bereavement on family members, lack of attention to outcome beyond the first year of bereavement, and a tendency for researchers to make idiosyncratic decisions about the selection of predictor variables and the measurement of outcomes, rendering it difficult to compare studies.

While awaiting the results of systematic studies, clinicians may use knowledge that we already possess to help the individual who has been bereaved because of suicide. We have found no comparative studies that examine the types of help that these individuals prefer or the comparative efficacy of different types of therapy that they may receive. However, there are anecdotal reports about support groups. Some observers have found that the members of "suicide survivor" peer groups feel a profound sense of relief at being able to tell their stories (29, 60, 61) and that there may be improvement over time in symptoms of depression, emotional lability, concentration, and capacity to function as parents or students. In thinking of such a referral, one must bear in mind that those who participate in such groups may be self-selected individuals who are particularly articulate, communicative, and willing to share their difficulties.

The following might be useful guidelines for persons who work with individuals bereaved as a result of suicide. First, these survivors never resolve their feelings entirely. Therefore, overly ambitious therapeutic goals in this direction may frustrate rather than help the bereaved individual. Therapists should be particularly attuned to conscious and unconscious feelings of guilt due to anger or to perceived failures to save the deceased person (62, 63). Second, some of these bereaved individuals may respond positively to peer group experiences. Third, a family history of suicide should be asked about in interviewing any patient, since some patients may be reluctant to reveal this information. Such a family history may be related to current feelings of distress. Finally, if a patient commits suicide while in therapy, one should make an active effort to talk with the family. Such support at this crucial time may have long-lasting benefit for the family members, not to mention the clinician. We hope that future research will add to our understanding of those who have been bereaved as a result of suicide and will suggest additional ways of helping them.

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# An Evaluation of a Mental Health Program for Homeless Men

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*The authors report the results of a before-and-after evaluation of an on-site mental health day treatment program for homeless men. Thirty-two subjects were interviewed 6 or more months after placement from a crisis shelter to community housing in order to probe housing stability, aftercare treatment compliance, employment, rehospitalization, and criminal justice contacts. In the after phase, living on the street was virtually eliminated, use of shelters decreased sevenfold, aftercare utilization tripled, and contacts with the criminal justice system were halved. Psychiatric hospitalizations and unemployment were higher in the* after *phase. Findings are discussed in relation to the need to conduct controlled experiments of new psychosocial treatments for the homeless mentally ill.*

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Surveys of the adult homeless in the United States have established that the seriously mentally ill are legion among their ranks. It has been estimated that from one-quarter to one-third of adult homeless have histories of psychiatric hospitalizations or are in need of psychiatric treatment (1–6). Many believe that the mentally ill who are homeless are in that situation because they have slipped through the mental health bureaucracy or have been poorly served by it (7, 8). It has been alleged that deinstitutionalization policies have resulted in patients being discharged from hospitals without adequate housing placement, ongoing supervision, or referral to community-based aftercare treatment (1, 9–12). Patients have ended up in the streets or in crisis shelters for the homeless.

Mental health policy makers and program planners have responded to the unique needs of the homeless mentally ill by developing innovative service programs for this constituency (13). An important program model involves the delivery of psychiatric and rehabilitative care *on-site* in the crisis shelter setting to maximize the involvement of those in need. To date, this program model has not been experimentally tested, and there is little information about its costs and benefits to guide future planning. In this paper we present findings of a before-and-after evaluation of an on-site mental health program for sheltered homeless men.

The Department of Psychiatry of Presbyterian Hospital in the City of New York is actively involved in providing mental health day treatment services to men housed at the Washington Heights Armory Municipal Shelter, directly across the street from Presbyterian Hospital in upper Manhattan. The department sponsors the Psychiatry Shelter Program, whose multidisciplinary team provides psychosocial counseling, recreational therapy, medication maintenance, and housing placement to men with psychiatric problems who are referred by the social service staff operating the shelter. Approximately 75 men are enrolled in the program at any time, with an average length of stay of about 5 months.

The Psychiatry Shelter Program's staff share the entire caseload, allowing for eight staff relationships to develop for each patient. Treatment plans, fashioned with the patients' participation, have as their goal to develop the patients' social skill level, i.e., their ability to relate to mental health professionals and to each other, and to cope in ways that do not perpetuate their

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condition. The following case material illustrates how the program functions.

## CASE REPORTS

*Case 1.* Mr. A, a 35-year-old single white man, entered the shelter system when he moved out of his brother's apartment due to frequent arguing between them. A college graduate, he had worked in various semiskilled and unskilled jobs but had difficulties taking criticism from bosses, resulting in erratic attendance. After losing a job, he came to the shelter to escape his brother's criticism that he was not doing enough and to try to become more independent. He was referred to the Psychiatry Shelter Program 6 months after living in the shelter; at the time of referral he complained of chronic depression, anxiety, and a lack of social contacts. He was diagnosed as suffering from dysthymic disorder with recurrent superimposed major depression, possible panic disorder, and avoidant personality disorder. He did not abuse drugs or alcohol. He had undergone brief psychotherapy in the past but was never treated with medication.

Mr. A quickly became engaged in the program, taking part in group therapy, recreation activities, the work program, and intensive case management for his housing and financial needs. He was placed on a regimen of desipramine, 250 mg/day, for his depression and panic attacks. He became less depressed, less anxious, and less socially isolated, and his appearance improved noticeably. In the fourth month of treatment, he was accepted into an adult home. He continued to attend the Psychiatry Shelter Program for a short time until beginning a day program in an outpatient psychiatric center.

*Case 2.* Mr. B, a 31-year-old single black man, had had several psychiatric hospitalizations for chronic schizophrenia and substance abuse since the age of 16. During one decompensation, he slashed his throat in response to command hallucinations. He dropped out of high school but received a General Equivalency Diploma in prison, where he served terms for auto theft and unarmed robbery. He had abused alcohol, phencyclidine, intravenously administered heroin, and cocaine in the past.

Despite his history, Mr. B was mild-mannered, likeable, and somewhat withdrawn when he was not abusing street drugs and was stabilized on a regimen of prescribed medication. He came from a large, intact, working-class family. His parents died several years ago, but he remained close to a brother and sister. He had worked for brief periods in unskilled or semiskilled jobs and had maintained his own single room. When he was fired from his last job, he moved into the shelter. Just before starting in the Psychiatry Shelter Program, he was drinking two to three pints of liquor a day and he tried "crack" for the first time. He began to hear voices again, so he voluntarily entered a psychiatric hospital where he was detoxified from alcohol and stabilized on a regimen of orally administered haloperidol and thiamine. He was discharged to his sister's apartment but stayed there only on weekends, living in the shelter during the week.

In the Psychiatry Shelter Program, Mr. B was switched to the decanoate form of haloperidol. He did not use drugs or alcohol and remained stable for 9 months. During this period, case workers contacted his sister and enlisted her help in supporting Mr. B's efforts to avoid drugs and continue his medication regimen. When she moved to another apartment, the patient moved into her vacated one full-time. He received welfare and attended a university-affiliated outpatient day program within walking distance of his apartment. He continued to attend the program periodically to visit with staff, sit in on groups, and socialize with other patients.

## METHOD

In an initial attempt to evaluate the efficacy of the Psychiatry Shelter Program, we elected to contact all individuals who were placed in community-based housing from the program's inception in the summer of 1986 to January 1988 (N=39 men). By contrasting the life situations of the men 6 months before they entered the program and 6 months after termination, we hoped to learn how the program has worked for those who were able to emerge from homelessness.

Over 200 men attended the program in the time period under study. Fifty persons remained involved long enough to undergo discharge planning. Thirty-nine were placed in community housing, eight were transferred for psychiatric inpatient care, and three were transferred to other shelters for the homeless. Of the 39 men discharged to community living arrangements, approximately equal proportions (about one-third) were discharged to their own apartments, family settings, and adult homes.

An interview schedule was developed to elicit social background data and information on living arrangements, financial support, psychiatric inpatient and outpatient treatment, employment, and criminal justice contacts in the 6-month period before program entry and the 6-month period after discharge to community housing. Data on psychiatric diagnosis (*DSM-III*), based on the clinical assessment of the program psychiatrist, were obtained from the case record. The case record was also the source of information on length of stay and program participation.

In the summer of 1988, attempts were made to locate and interview the 39 men placed in community housing. Finding a person's whereabouts was accomplished with information in case records, reports from family members, and the assistance of staff of mental health treatment programs. On occasion, the computer files of the municipal agency responsible for operating public shelters were used to locate patients currently living in shelters.

Patients were initially contacted by mail to request their participation in the study. When they agreed to be interviewed, they signed a form acknowledging voluntary informed consent. Subjects were paid an incentive of $10.00 upon completion of the interview. It was possible to obtain adequate information for 32 men (82%). Only one refused to be interviewed, and four could not be located. Two deaths occurred in the 6-month period afer discharge; one was a homicide, and the other resulted from complications of diabetes and chronic lung disease.

The research interview relied heavily on the subject's

**TABLE 1. Characteristics of 32 Homeless Men During 6 Months Before Entering the Psychiatry Shelter Program and 6 Months After Community Placement**

| Characteristic | Before | After |
|---|---|---|
| Men who lived on streets at any time | 4 | 0 |
| Criminal justice contacts | 4 | 2 |
| Men who lived in shelters at any time | 20[a] | 3 |
| Days in shelter | 1,831 | 265 |
| Men admitted to psychiatric hospital | 9 | 12 |
| Days in hospital | 724 | 802 |
| Men who attended aftercare treatment | 10 | 20 |
| Aftercare visits | 286 | 843 |
| Men with no income | 10 | 0 |
| Men employed at any time | 7 | 3 |

[a] The remaining 12 subjects either were living in an institutional setting or were domiciled before entering the shelter. They were admitted to the Psychiatry Shelter Program very soon thereafter.

self-report of activities, including use of hospital and aftercare services. When possible, such information was checked with case record data.

## FINDINGS

### *Demographic and Clinical Characteristics*

At the time of entry into the program, the majority of the 32 interviewed men were single (94%, N=30), unemployed (87%, N=28), of minority status (78% [N=25] were black or Hispanic), and in their thirties (median age=32 years). Sixty-three percent (N=20) were high school graduates, and 25% (N=8) had some college experience. Nineteen percent (N=6) had served in the armed forces. Forty-four percent (N=14) had jail or prison histories for offenses ranging from misdemeanors (jumping subway turnstiles, trespassing) to felonies (arson, manslaughter).

Eighty percent (N=26) had at least one prior psychiatric hospitalization. Schizophrenia/schizoaffective disorder was the most common psychiatric diagnosis, found in 69% (N=22) of the study subjects. Co-occurring substance abuse problems were present in 63% (N=20). Polydrug abuse was most frequent, followed by cocaine/crack and alcohol.

### *Before-and-After Comparisons*

Before-and-after comparisons of variables of central interest in this investigation are shown in table 1. Important differences are apparent when conditions present in the period 6 months after the men's discharge are contrasted with conditions present 6 months before their entry into the program. There was a marked reduction in the number of people living on the streets and in shelters for the homeless in the after period. In fact, the total days spent in shelters was reduced sevenfold. There was also a marked reduction in the number of criminal justice contacts in the after phase. It is notable that the number of study subjects who participated in psychiatric aftercare treatment doubled in the after period. Moreover, the total number of aftercare visits increased threefold in the after phase. The number of men with no income decreased markedly in the after period.

In the before phase, nine men experienced psychiatric hospitalizations; only four of these men did not experience hospitalization in the after phase. Seven of the men hospitalized in the after phase had not been hospitalized in the before phase. The number of men employed at some time decreased by more than 50% in the after phase.

### *Factors Related to Rehospitalization, Homelessness, and Aftercare Attendance*

In an effort to better understand rehospitalization, homelessness, and aftercare attendance in the after phase, these outcomes were explored in relation to psychiatric diagnosis. Although the numbers are small, the findings suggest areas to be studied more thoroughly in the future. Eleven of the 12 patients who were hospitalized in the after phase had a diagnosis of schizophrenia/schizoaffective disorder. Sixty-seven percent of these patients (N=7) also abused drugs or alcohol. The three patients who experienced homelessness in the after phase had co-occurring schizophrenia and substance abuse.

It is notable that 78% of the patients who returned to family living settings (N=7 of 9) were rehospitalized in the after period, in contrast to 30% of those who lived in their own apartments (N=3 of 10) and 8% of those in community residences (N=1 of 13). Only half (N=5) of the patients who returned to family settings attended aftercare, in contrast to 80% (N=8) of the patients who returned to their own apartments and 67% (N=9) of those who lived in community residences. Twenty percent (N=2) of the patients discharged to their own apartments experienced homelessness in the after period, in contrast to 11% (N=1) of those in family settings. No patients in community residences were homeless in the after period.

## DISCUSSION

The pilot study reported here demonstrates that persons who were placed out of an on-site day treatment program for homeless men could be tracked and evaluated for a treatment outcome study. Findings identified areas in which the program appears to have a strong impact. Homelessness (street or shelter living) and criminal justice contacts were markedly reduced, and patients had more contact with the mental health delivery system and better income entitlements. The potential importance of these findings for mental health policy and program planning demands that the study be replicated with a larger sample.

There were several rather surprising results. Of all persons hospitalized in either the before or after phase of the study, only three were hospitalized solely in the before phase. The increased hospitalization rate in the after phase requires confirmation and, if real, it must be understood.

Rehospitalization findings could indicate success or failure. On one hand, greater use of the psychiatric hospital in the after phase might reflect the patients' increased awareness of their psychiatric illnesses and need for treatment. On the other hand, rehospitalization can result from inadequately treated co-occurring substance abuse problems. None of the patients in this study was being treated specifically for drug or alcohol abuse. Substance abuse among psychiatric patients has been associated with more frequent hospitalizations (14–16).

The discharge living arrangement is important in relation to subsequent rehospitalization and homelessness. Findings suggest that patients living in community residences fare much better. The men we studied experienced considerable residential instability in the period before becoming homeless. Forty-seven percent (N=15) lived with family members (parent, partner, sibling, or other relative) during that time. Twenty-eight percent were living with their families 6 months after leaving the Psychiatry Shelter Program; and of this group, 78% required rehospitalization. It is possible that for *these* men, some aspect of living with the family was related to rehospitalization. Supporting this notion is the finding from family studies of schizophrenia that when a patient returns to a family setting with high expressed emotion, the chances of relapse are increased (17). In such families, psychosocial interventions in conjunction with neuroleptics can decrease the relapse rate (17–19). Before any conclusion can be drawn on this important subject, however, it would be necessary to determine if the men who returned to their families were sicker than the other men in our sample. Community residences tend to be highly selective and do not admit patients who might be high risks for rehospitalization.

The decrease in the number of people employed in the after phase also needs further study and evaluation. Most patients (N=29 of 32) were receiving Supplemental Security Income (SSI) in the after phase. While 94% of the patients (N=30) had worked at some time in their lives, only three were employed in the after phase. Some contend that SSI is a disincentive for gainful employment among the disabled. It is of interest that when asked to comment on what else the Psychiatry Shelter Program might do to be helpful to program participants, many men mentioned work rehabilitation.

Because the homeless mentally ill are among the most difficult patients to engage and hold in treatment, successful program models for this constituency are urgently needed. Indeed, well-designed and replicated controlled experiments involving new psychosocial treatments are necessary (20, 21). The study reported here is a step in that direction and underscores the feasibility and importance of such efforts.

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# Clinical Correlates of the Deficit Syndrome of Schizophrenia

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*The authors propose using primary and enduring negative or deficit symptoms for dichotomizing schizophrenic patients into two groups, deficit and nondeficit. The validity of this approach was examined by comparing 17 deficit and 17 nondeficit patients for differences in premorbid adjustment and degree of neurological impairment. Deficit patients were characterized by poorer premorbid adjustment and greater neurological impairment. Neurological impairment was not related to premorbid adjustment in either group or in the total patient population. These findings support the utility of deficit symptoms for defining a more homogeneous subgroup of schizophrenia.*

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Schizophrenia is characterized by marked variance among patients in age at onset, clinical presentation, course, treatment response, and other associated features. It is likely that this observed clinical variability is related to heterogeneity in both etiology and pathophysiology. In light of this hypothesized heterogeneity, investigators have used differences in the patterns of clinical symptoms to try to define subgroups of a more homogeneous nature. In this regard, primary and enduring negative or deficit symptoms have been proposed as symptoms suitable for dichotomizing schizophrenic patients (1, 2).

The concept of deficit symptoms is derived from Kraepelin's original description of the consequences of the "weakening of those emotional activities which permanently form the mainspring of volition" (3). The presence of these symptoms is hypothesized to represent the existence of a specific pathophysiological process that is independent of the processes underlying the production of psychotic or other symptom complexes (2). Previous investigations of patients with deficit and nondeficit forms of schizophrenia have revealed a differential impairment on neuropsychological testing, eye tracking, and measures of social and physical anhedonia (4–6), providing preliminary data on the validity of this distinction.

There are several reasons to be interested in the relationships among the deficit/nondeficit distinction, premorbid adjustment, and neurological impairment. First, there is extensive overlap between the concept of process schizophrenia and the negative symptom concept, suggesting that patients with poor premorbid adjustment are more likely to have negative symptoms as part of their clinical picture (7). Indeed, several studies have found an association between negative symptoms and poor premorbid adjustment (8–12). Second, in a retrospective examination of twin studies, the presence of negative symptoms and poor premorbid adjustment in the proband twin increased the diagnostic concordance of monozygotic twins (13), suggesting that poor premorbid adjustment may be integrally related to the development of persistent negative symptoms (13, 14).

Interest in the degree of neurological impairment in deficit patients emanates from the demonstration of greater brain pathology in patients with negative symptoms. Enlarged ventricle-brain ratios (VBRs) (8, 15–17), decreased metabolic activity in the frontal cortex (18), and impaired performance on neuropsychological testing (19, 20) have been found to be associated with negative symptoms. Further, neurological abnormalities have been previously found to be associated with withdrawal (21) and blunted affect (22). However, there have been conflicting results (23–27). The use of deficit symptoms, which are longitudinally assessed, may be more valuable for subgrouping patients with schizophrenia than cross-sectionally obtained measures of negative symptoms, since the latter approach combines the assessment of both primary (i.e., reflecting schizophrenia) and secondary (i.e., reflecting depression, drug effects, and so forth) negative symptoms (1, 28). The contradictory findings of studies concerning the validity of the use of negative symptoms for subgrouping schizophrenic patients may be due, in part, to the failure to distinguish primary from secondary negative symptoms.

The current study was designed to test the hypothesis that deficit patients are characterized by poor premorbid adjustment and more neurological impairment

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and to examine the relationship between these clinical features.

## METHOD

Thirty-four patients with *DSM-III* schizophrenia were selected from an outpatient research clinic for entry into the study. The patients were subgrouped into deficit (N=17) and nondeficit (N=17) types on the basis of the consensus diagnosis of two psychiatrists (R.W.B. and B.K.) who used the Schedule for the Deficit Syndrome (29). This schedule provides specific criteria for the categorization of schizophrenic patients into deficit and nondeficit groups. The categorization of patients into deficit and nondeficit subtypes requires the clinical differentiation of primary, enduring negative symptoms from transient and secondary negative symptoms. Interrater reliability data for global categorization (unweighted kappa=0.73) and for each of the six negative symptoms (weighted kappas=0.60 to 0.74) (29) suggest, however, that this discrimination can be reliably made by trained clinicians. All patients were interviewed while they were between episodes and at their clinical baseline. Additional information, if needed, was obtained from clinicians with longstanding contact with the patients and from family members. Each deficit patient was matched by race and gender to the nondeficit patient with the closest clinic admission date.

Premorbid adjustment and degree of neurological impairment in the deficit and nondeficit patients were evaluated with the Premorbid Adjustment Scale (30) and the Neurological Evaluation Scale (31). The Premorbid Adjustment Scale was designed to assess premorbid adjustment from a developmental context and is a modification of previous scales used with inpatients and outpatients (30). The scale provides for the assessment of social, scholastic, and sexual development in four distinct age periods: childhood (through age 11), early adolescence (ages 12–15), late adolescence (ages 16–18), and adulthood (age 19 and older). In addition, the scale has a general section that includes measures of premorbid function, symptoms, and assessments of lifetime function. A score is obtained for each age period subscale and the general subscale. A total score is calculated by averaging all of the subscale scores rated for the patient. Since the general subscale is not strictly a measure of premorbid function, the total score was calculated both with and without this subscale. Information for completing the scale was obtained from the patient, family members, and review of past medical records.

The Neurological Evaluation Scale comprises 26 items designed to assess the intactness of three functional areas of interest: sensory integration, motor coordination, and sequencing of complex motor acts; it also assesses frontal release signs, selective brief indicators of eye movement abnormalities, and short-term memory. The results of the scale are presented as the number of total signs and the number of signs for each subscale, and as the total score and the score for each subscale; the latter method takes into account the severity of impairment. The interclass correlation coefficients for each of the subscales ranged from 0.63 to 0.99 (31). The premorbid adjustment and neurological evaluations were completed by either master's or doctoral level clinicians who were trained in the use of the instruments and were blind to the deficit/nondeficit categorization and study hypotheses.

## RESULTS

The 17 deficit and 17 nondeficit patients were similar with respect to demographic variables, medication status, age at onset, and duration of illness. The mean±SD ages for the two groups were 32.6±8.4 and 30.8±7.8, respectively. Both groups consisted of 14 men and three women, nine of whom were black and eight of whom were white. Fourteen patients in the deficit group and 16 patients in the nondeficit group were taking medication. The mean±SD ages at onset for the two groups were 21.7±7.7 and 22.4±5.1 years; the mean±SD durations of illness were 11.0±6.0 and 8.6±4.6 years.

In the deficit cohort, premorbid adjustment was significantly worse in the childhood and early and late adolescence age periods, in the general score subscale, and in the total score measures both including and excluding the general score subscale. The results of analysis of variance (ANOVA) for each age period, the general scale, and the total score are presented in table 1. In each case the ANOVA did or did not use the assumption of equal variance, depending on the results of the Levine test for equal variance. Although the difference between the deficit and nondeficit patients for the adult age period was not significant, the difference between the two groups was similar in magnitude and direction to the differences for the earlier age periods. An item-by-item analysis revealed that the deficit patients were more impaired on each of the items from the four age periods, suggesting that the difference between deficit and nondeficit patients was not attributable to a few items differentiating the two groups. On the items making up the general subscale, the deficit patients were more impaired on the items assessing global function, including those which overlap conceptually with deficit symptoms, i.e., the items assessing motivation, interest, and social-personal adjustment.

The comparison of the results of the neurological evaluation of the two groups revealed that the deficit patients were more neurologically impaired than the nondeficit patients, as assessed by either the total number of signs or the total score (see table 1). The most prominent difference was in the area of sensory integration, which includes the items stereognosis, graphesthesia, right-left confusion, the face-hand (bilateral extinction) test, and audiovisual integration. As can be seen from table 1, there were significant differences

**TABLE 1. Premorbid Adjustment and Neurological Ratings of Patients With Deficit and Nondeficit Forms of Schizophrenia**

| | Deficit Patients (N=17) | | Nondeficit Patients (N=17) | | | |
|---|---|---|---|---|---|---|
| Scale and Item | Mean | SD | Mean | SD | F (df=1, 32) | p |
| Premorbid Adjustment Scale scores | | | | | | |
| Childhood | 0.40 | 0.16 | 0.27 | 0.16 | 5.73 | 0.02 |
| Early adolescence | 0.39 | 0.17 | 0.28 | 0.12 | 5.18 | 0.03 |
| Late adolescence[a] | 0.49 | 0.22 | 0.29 | 0.17 | 8.16 | 0.008 |
| Adulthood[b] | 0.45 | 0.23 | 0.31 | 0.17 | 2.46 | 0.13 |
| General | 0.46 | 0.18 | 0.30 | 0.19 | 6.15 | 0.02 |
| Total without general | 0.42 | 0.16 | 0.28 | 0.12 | 8.25 | 0.007 |
| Total with general | 0.44 | 0.15 | 0.29 | 0.12 | 9.84 | 0.004 |
| Neurological Evaluation Scale | | | | | | |
| Number of signs | | | | | | |
| Total | 11.53 | 3.48 | 8.94 | 4.28 | 3.74 | 0.06 |
| Sequence | 1.59 | 1.66 | 1.65 | 1.37 | 0.01 | 0.91 |
| Motor | 1.12 | 0.70 | 1.18 | 0.95 | 0.04 | 0.84 |
| Sensory | 3.29 | 1.10 | 1.47 | 1.12 | 22.75 | <0.00001 |
| Other | 5.53 | 1.42 | 4.65 | 2.03 | 2.16 | 0.15 |
| Total and subscale scores | | | | | | |
| Total | 20.88 | 8.19 | 15.59 | 9.45 | 3.04 | 0.09 |
| Sequence | 2.82 | 3.23 | 3.24 | 3.61 | 0.12 | 0.73 |
| Motor | 1.76 | 1.09 | 1.47 | 1.12 | 0.60 | 0.44 |
| Sensory | 6.24 | 3.35 | 2.41 | 2.12 | 15.83 | 0.0004 |
| Other | 10.06 | 3.23 | 8.47 | 4.87 | 1.25 | 0.27 |
| Sensory integration scores | | | | | | |
| Audiovisual integration | 1.65 | 0.70 | 0.82 | 0.95 | 8.25 | 0.007 |
| Stereognosis | 0.47 | 0.87 | 0.12 | 0.33 | 2.42 | 0.13 |
| Graphesthesia | 2.00 | 1.62 | 0.65 | 1.11 | 8.05 | 0.008 |
| Face-hand test | 0.47 | 0.72 | 0.06 | 0.24 | 5.03 | 0.032 |
| Right-left confusion | 1.65 | 0.61 | 0.76 | 0.90 | 11.18 | 0.002 |

[a] N=14 deficit patients; df=1, 29.

[b] N=7 deficit patients and 14 nondeficit patients; df=1, 19.

between the two patient groups on four of the five items.

The relationship between neurological impairment and premorbid adjustment was examined in the deficit and nondeficit patients separately and with the two groups combined. Neither the Neurological Evaluation Scale total score nor the total number of signs was significantly correlated with the total score on the Premorbid Adjustment Scale or any of its subscales.

## DISCUSSION

The results of this investigation suggest that deficit patients are characterized by poorer premorbid adjustment and are more neurologically impaired than nondeficit patients. The difference between deficit and nondeficit patients on measures of premorbid adjustment existed across three of the four age periods, the general scale, and the total score of the Premorbid Adjustment Scale. The difference in neurological impairment was observed primarily in the functional area of sensory integration. These results, in combination with previous studies of deficit patients (4–6), support the validity of subgrouping patients on the basis of the presence or absence of deficit symptoms.

The relationship between poor premorbid adjustment and the presence of deficit symptoms is consistent with previous studies that reported an association between negative symptoms and poor premorbid adjustment (8–13). There are a number of methodological issues in the current study which would support the contention that the difference between the two groups is not artifactual. First, the use of family members and past hospital records, as additional sources of information, would tend to minimize any systematic differences in the ability of deficit and nondeficit patients to provide information about their premorbid history. Second, previous studies have suggested that premorbid adjustment varies with sex and age at onset (13, 32, 33). In this study, the age at onset and the ratio of men to women was the same in both groups, suggesting that the differences between the two groups were not due to these factors. The association between poor premorbid adjustment and deficit symptoms and the earlier suggestions that poor premorbid adjustment may be the precursor of negative symptoms argue that 1) aspects of poor premorbid functioning in schizophrenia represent the early onset of deficit symptoms, and 2) deficit patients represent a subgroup of schizophrenic patients characterized by a disease process with an onset before adolescence.

Deficit patients were differentiated from nondeficit patients primarily by greater impairment on items related to sensory integration. In contrast, there were no differences between the two groups on the subscales related to motor coordination and sequencing of complex motor acts. Further, the degree of impairment on the sensory integration items exhibited by the nondeficit patients was comparable to that observed in normal control subjects (31). These results suggest that although the two groups share common impairments, patients with deficit symptoms have an additional impairment in sensory integration. The significance of this impairment is unclear; however, since these items are thought to reflect parietal lobe function (34), a hypothesis positing a role for the parietal cortex in the neuroanatomical substrate underlying the production of deficit symptoms is suggested. Such a hypothesis would be amenable to testing by neuropsychological examination and functional and structural brain imaging. Indeed, we have previously reported preliminary positron emission tomography scan data demonstrating a differential pattern, between patients with and without deficit symptoms, of glucose utilization in the parietal cortex (35).

Neurological signs were not correlated with poor premorbid adjustment in either the deficit or nondeficit patients or in the total patient sample. A larger group of patients would be required to exclude the possibility of an interaction between these variables. Three previous studies have also failed to find such an association (27, 36, 37). The sole study that did find a relationship between neurological signs and premorbid adjustment was that of Quitkin et al. (38), who compared the degree of neurological impairment in schizophrenic patients with premorbid asociality and in a group of patients with mixed subtypes of schizophrenia who had normal premorbid social development. They found that the former group had more neurological signs. A possible explanation for these apparently contradictory findings is that Quitkin et al. used premorbid adjustment as a categorical variable and thus did not directly assess the correlation between poor premorbid adjustment and neurological signs. These schizophrenic patients with premorbid asociality may substantially overlap with the deficit patients in the current study, and the finding of more neurological signs in the patients with premorbid asociality may be related to a high rate of deficit symptoms in these patients, a possibility that is plausible, since diminished social drive is a deficit symptom. Indirect support for this argument is provided by the fact that two of the signs which differentiated the two groups in the Quitkin et al. study were measures of sensory integration—agraphesthesia and the face-hand test. Quitkin et al. did not provide information about the degree of negative symptoms in the two groups of schizophrenic patients, so the validity of this argument remains speculative.

The results of the present study require confirmation in larger study populations. If they are confirmed, important questions arise concerning the mechanism of greater neurological impairment and the nature of the underlying neural substrate of deficit symptoms. Future studies using structural and functional imaging techniques, neuropsychological testing, and other measures should provide important information on the anatomical regions involved in the pathogenesis of these symptoms.

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# Subjective Awareness of Abnormal Involuntary Movements in Chronic Schizophrenic Patients

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*The authors examined the effects of verbal and visual feedback on subjective awareness of involuntary movements in 20 chronic schizophrenic patients. At initial evaluation only 25% of the patients were fully aware of their movement disorder. Both verbal and visual feedback resulted in significant immediate enhancement of awareness. However, assessment of awareness 2 weeks later showed a return to prefeedback baseline levels. Lack of awareness of involuntary movements was associated with a lack of awareness of psychiatric disorder, and both were associated with a longer duration of illness.*

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It is well recognized that long-term neuroleptic treatment is associated with the risk of developing tardive dyskinesia, a potentially persistent neurological syndrome. Thus, it has been recommended that patients be informed of this risk when they are prescribed neuroleptic treatment (1, 2). In order to participate rationally in assessing the risk-benefit ratio involved in long-term neuroleptic treatment, a patient should, at minimum, be able to understand and retain the relevant information. Further, when tardive dyskinesia is already manifest, the patient should be aware of its presence. However, patients with tardive dyskinesia are often not aware of their involuntary movements or, if aware, appear not to be concerned about them (3–7). In spite of its importance for rational policy making, this lack of awareness of involuntary movements has received limited formal study. In particular, little is known about the temporal stability of lack of awareness of these movements, its relation to lack of awareness of psychiatric illness, and whether such awareness can be enhanced by advisement procedures.

The primary aim of this study was to determine whether verbal or visual feedback to patients would enhance their subjective awareness of abnormal involuntary movements and, if so, whether the improved awareness would be maintained over a 2-week follow-up period. We also examined the relation of lack of awareness of involuntary movements to awareness of psychiatric disorder to determine whether the former reflects a discrete abnormality or is part of a generalized pathology of insight.

## METHOD

The study was conducted at the Creedmoor Psychiatric Center research unit, affiliated with the New York State Psychiatric Institute. All patients gave informed consent for participation in research and were evaluated for the presence of involuntary movements as part of ongoing research protocols. Those with mental retardation, alcohol or drug dependence, significant medical disorders, and organic brain syndromes were excluded from participation.

All schizophrenic patients (diagnosed according to *DSM-III*) at the unit who manifested involuntary movements were recruited for this investigation. A *DSM-III* diagnosis of schizophrenic disorder was assigned on the basis of independent evaluations by two research psychiatrists. There was no instance of diagnostic disagreement. The sample comprised 13 male and seven female patients. Their mean±SD age was 33.9±6.4 years, their mean duration of illness was 14±6.4 years, they had a mean of 11.8±1.5 years of formal education, and their mean current full-scale IQ was 82.5±8.8. There was no significant difference between the sexes in any of these variables. Although the exact cumulative duration of neuroleptic treatment could not be determined reliably, all patients had received neuroleptic treatment for more than 3 years.

At the time of admission to the research unit, patients are routinely briefed by their treating psychiatrist on the risk of tardive dyskinesia and their involuntary movement status. They then undergo repeated

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evaluations of involuntary movements in research protocols. In this study, involuntary movements were assessed independently by two research psychiatrists (G.C. and S.D.R.), and the findings were recorded on the Rockland Tardive Dyskinesia Scale (8).

The initial phase of the study comprised three stages. First, patients were asked if they had ever heard of tardive dyskinesia or involuntary movement disorders associated with neuroleptic treatment. The two research psychiatrists independently rated the responses as yes or no. There was no instance of interrater disagreement on this item. This was followed by a standardized examination to assess involuntary movements. The interrater reliability (intraclass correlation coefficient [ICC]) for global severity of abnormal involuntary movements was 0.96. Patients were then interviewed to assess their awareness of the presence and localization of their involuntary movements.

When a patient denied awareness of, or incompletely described, the involuntary movements, these were described to the patient (verbal feedback) and awareness was reassessed. If lack of awareness persisted, the patient was asked to stand in front of a mirror (72 in.×16 in.), the movements were pointed out (visual feedback), and awareness was again assessed. The duration of visual feedback was sufficient for manifest movements to be observed by the patient. At each step, the two research psychiatrists independently rated awareness of involuntary movements using a 3-point scale on which 3 indicated full awareness of the presence and bodily distribution of movements, 2 indicated incomplete or inconsistent awareness, and 1 indicated a complete lack of awareness. Interrater reliability was consistently high across the three ratings ($ICC=0.92$ to $0.98$). Finally, awareness of psychiatric disorder was assessed by direct inquiry and rated as present or absent. There was no instance of interrater disagreement on this item.

Subjective awareness of the presence and localization of involuntary movements, knowledge of tardive dyskinesia, and awareness of psychiatric illness were reassessed 2 weeks after the initial evaluation. All patients were in a stable state with chronic residual psychotic symptoms (the mean±SD total score on the Brief Psychiatric Rating Scale was 50.9±7.6; the Clinical Global Impression scores ranged from 3 to 6). No patient showed a change greater than 1 point on the Clinical Global Impression scale across the two evaluation periods. All patients were receiving stable doses of neuroleptics (range=500–2000 mg in chlorpromazine equivalents) during the study period.

## RESULTS

The mean±SD global severity rating of involuntary movements was 2.3±0.8 at baseline and 2.4±0.8 at follow-up and ranged from mild to moderate. All patients met the criteria of the Research Diagnoses for Tardive Dyskinesia (9). Five (25%) of the patients recalled having heard of tardive dyskinesia or abnormal involuntary movements associated with neuroleptic treatment. Only five (25%) of the patients were fully aware of their involuntary movements at initial evaluation, four (20%) showed partial awareness, and 11 (55%) showed complete lack of awareness.

**TABLE 1. Awareness of Abnormal Involuntary Movements in 20 Schizophrenic Patients**

| Time of Measurement | Patients Fully Aware N | Patients Fully Aware % | Patients Incompletely Aware N | Patients Incompletely Aware % | Patients Totally Unaware N | Patients Totally Unaware % |
|---|---|---|---|---|---|---|
| Baseline | 5 | 25 | 4 | 20 | 11 | 55 |
| Immediately after verbal feedback | 7 | 35 | 7 | 35 | 6 | 30 |
| Immediately after visual feedback | 10 | 50 | 8 | 40 | 2 | 10 |
| At 2-week follow-up[a] | 6 | 32 | 4 | 21 | 9 | 47 |

[a] N=19.

Both verbal and visual feedback resulted in a significant increase in reported awareness of involuntary movements. The mean±SD awareness score increased from 1.7±0.9 at baseline to 2.1±0.8 after verbal feedback (paired $t=2.8$, $df=19$, $p<0.01$) and to 2.4±0.7 after visual feedback (paired $t=4.3$, $df=19$, $p<0.001$). The changes were consistently in the direction of increasing awareness of abnormal involuntary movements (see table 1).

Two-week follow-up evaluations were completed for 19 patients. One patient initially rated as unaware of both involuntary movements and psychiatric disorder refused to cooperate with further evaluations. The increment in awareness noted following the feedback procedures was not sustained over the follow-up period; the mean±SD awareness score fell back to 1.8±0.9. The changes were consistently in the direction of decreasing awareness from the end of feedback at the initial session to follow-up (see table 1). The decrement was significant (paired $t=2.6$, $df=18$, $p<0.02$), and awareness scores at the initial baseline and follow-up evaluations were significantly correlated ($r=0.80$, $df=18$, $p<0.001$). Of the five patients who were initially rated as fully aware of their involuntary movements, four were found to be fully aware and one was partially aware at follow-up. All nine patients rated as completely unaware of their movements at follow-up had also been given this rating at baseline.

At follow-up nine (47.4%) of the 19 patients recalled ever having heard of tardive dyskinesia. This group contained all five patients who recalled having heard of tardive dyskinesia at the initial evaluation. The other 10 patients remembered meeting with the research psychiatrists 2 weeks earlier but could not recall the specific content of the discussion.

Only seven patients admitted to having a psychiatric disorder at the initial evaluation. Awareness of psychiatric disorder was significantly associated with awareness of involuntary movements both at the initial evaluation ($t=3.5$, $df=18$, $p=0.003$) and at follow-up ($t=2.5$, $df=17$, $p<0.05$). At both evaluations longer duration of illness was associated with lack of awareness of involuntary movements ($r=-0.70$, $df=18$, $p=0.0005$, and $r=-0.62$, $df=17$, $p<0.01$, respectively) and lack of awareness of psychiatric disorder ($t=3.2$, $df=18$, $p<0.005$, and $t=3.1$, $df=17$, $p<0.01$, respectively). Although age and duration of illness were significantly correlated ($r=0.74$, $df=18$, $p<0.005$), at both evaluations age was only marginally related to awareness of involuntary movements ($r=0.48$, $df=18$, and $r=0.47$, $df=17$, respectively, $p=0.04$ for both) and to awareness of psychiatric disorder ($t=1.9$, $df=18$, $p=0.07$, and $t=2.1$, $df=17$, $p=0.05$). Neither measure of awareness was related to years of education or full-scale IQ.

At both baseline and follow-up evaluations awareness of involuntary movements was not related to severity of tardive dyskinesia when the global severity score was considered and when orofaciolingual and limb-axial scores were examined separately ($p>0.20$ for all comparisons). However, mean±SD orofaciolingual dyskinesia scores were significantly higher for those who were unaware of their psychiatric disorder ($5.4\pm4.5$) than for those who were aware ($1.7\pm1.1$) ($t=2.1$, $df=18$, $p<0.05$). However, such awareness was not related to limb-axial dyskinesia scores ($p>0.10$).

## DISCUSSION

The finding that 75% of our patients were completely or partially unaware of their abnormal involuntary movements is consonant with the 52%–88% reported in previous studies (5–7). Both verbal and visual feedback resulted in an immediate increase of such awareness. It should be noted that to be rated as fully aware, patients had to describe the location of their involuntary movements, and there was no contingency (e.g., reward for acknowledging awareness) attached to the procedures. Thus, it is likely that the enhancement of awareness immediately following feedback was a real effect. However, the improvement was not sustained over a 2-week follow-up period and, on the average, the patients returned to their baseline levels of awareness.

Although the patients were able to learn about their involuntary movements, there was impaired retention and recall of the learned information after 2 weeks. It has been found that schizophrenic patients show low recall performance after adequate mnemonic organization has been established at the encoding level and that they rapidly forget well-encoded information (10), and tardive dyskinesia has been reported to be associated with cognitive impairment (7, 11–13). A recent study (14) found that such impairment involves visual learning more than verbal learning. Nevertheless, our findings show that lack of awareness is not a static phenomenon and that awareness can be enhanced, albeit temporarily. A significant short-term increase in awareness of tardive dyskinesia following advisement was reported also by Brown et al. (15).

It is not understood why schizophrenic patients often are unaware of their involuntary movements. Various explanations have been proposed including, among others, psychological denial (5), cognitive impairment (12), and anosognosia associated with right hemispheric dysfunction (16). Unlike the findings in our previous study of diagnostically heterogenous psychiatric outpatients (6), awareness of involuntary movements was not related to greater severity of tardive dyskinesia in this study, and such awareness was also unrelated to orofaciolingual and limb-axial dyskinesia scores. The relation between lack of awareness of involuntary movements and lack of awareness of psychiatric disorder suggests that a common pathology of insight may be at issue. We found that both measures of lack of awareness were related to longer duration of illness, and young patients early in the course of their illness have been found to be more aware of their involuntary movements (17). These findings suggest that lack of awareness may, in part, be a function of the chronicity of schizophrenic illness. We did not conduct formal studies of cognitive function in our patients. Although lack of awareness was not related to lower full-scale IQ, orofaciolingual dyskinesia scores were higher for patients who lacked awareness of their psychiatric disorder, and orofaciolingual dyskinesia has been reported to be associated with greater cognitive impairment (12). If indeed cognitive impairment results in lack of insight, it is likely that this is a subtle effect, and a general measure of intellectual functioning, such as the full-scale IQ, may not be sensitive enough to detect it. Further research is needed to elucidate the neuropsychological and psychological processes that might contribute to lack of insight.

Our findings may have implications for the issue of informed consent by schizophrenic patients. Although schizophrenic patients have been found to retain little of the relevant information disclosed to them during an informed consent procedure (18), similar deficits of recall have been noted also in nonpsychiatric medical patients (19, 20) and in healthy relatives of psychiatric patients (21). The inability to recall information regarding tardive dyskinesia should not in itself be considered a sufficient basis for determining the capacity of schizophrenic patients to give informed consent. The finding that a majority of patients were unaware of their involuntary movements or psychiatric disorder is more of a problem. However, immediately following the advisement procedures, all but two patients in our study had some awareness of their abnormal involuntary movements. Thus, lack of awareness is not necessarily a stable characteristic, and it may be an error to consider lack of insight alone without taking into account its stability and response to feedback. Formal informed consent procedures that involve a single formal briefing or written information and that do not involve interactive feedback or do not consider the possibility that patients may have difficulty in retaining information under such conditions are clearly inadequate. Methods need to be developed that will enhance the insight of patients into their disabilities and allow them to participate more meaningfully in their own treatment.

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# Delusions in Newly Admitted Residents of Nursing Homes

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*Two psychiatrists, using standardized clinical examinations, found that 21% of 125 patients newly admitted to nursing homes had delusions. The psychiatric disorders associated with these delusions are described. Delusional patients were more behaviorally disturbed before admission than nondelusional patients. These behavior problems were often the reason for admission, and they persisted after admission. Nursing home staff members infrequently identified and often inappropriately treated delusional patients. Since delusions are an important potentially treatable cause of behavior problems in nursing home residents, the authors suggest ways to improve the recognition and management of delusions.*

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Previous cross-sectional studies of nursing home residents have demonstrated a very high prevalence of both behavioral problems and neuropsychiatric illness, especially dementia (1–3), in these residents. Unfortunately, research on dementia has largely ignored behavior problems, possibly because they are seen as secondary to cognitive problems or to personality changes and are therefore thought to be untreatable ( 3, 4). Delusions are rarely considered as a cause of behavior problems in dementia, although both Alzheimer and Kraepelin described delusions as part of the clinical picture in senile dementia (5–7). Furthermore, treatment studies and case reports indicate that behavior problems subside when delusions are treated (8–10).

We addressed the following questions in a sample of nursing home patients, most of whom were demented:

1. What is the prevalence of delusions in individuals newly admitted to nursing homes?
2. What is their phenomenology, and which psychiatric illnesses are they associated with?
3. Do delusional and nondelusional residents differ in terms of behavior problems before and after nursing home admission?
4. Do they differ in cognitive status and physical functioning?
5. Do nursing staff members recognize delusions, and what psychotropic medications are used to treat them?

## METHOD

Two hundred six new residents admitted consecutively to six intermediate-level-of-care nursing homes in the Baltimore area between November 1987 and March 1988 were contacted as part of a longitudinal study of adjustment in nursing homes. Only residents who had not been in a nursing home in the preceding 6 months were eligible for the study. For this reason, 37 of the newly admitted residents were excluded. In 44 other cases, the family or the resident refused consent or was unavailable for consent. The remaining 125 residents were enrolled in the study. The nonparticipating residents did not differ in terms of age, sex, and race from the study sample.

The study residents were examined within 4 weeks of admission by one of two research psychiatrists (R.K.M. and B.W.R.) using the Modified Present State Examination. This is a semistructured clinical examination whose validity and interrater reliability have previously been demonstrated for patients with stroke (11) and Alzheimer's disease (12). For this study, both research psychiatrists had been trained in its use. To assess interrater agreement, five randomly selected nursing home patients were examined. Three of these examinations were conducted by B.W.R. and two by R.K.M.; both psychiatrists were present for each examination. Each psychiatrist then independently recorded his diagnosis. The psychiatrists were in agreement on all five cases: there were three diagnoses of Alzheimer's disease, one of multi-infarct dementia, and one case with no psychiatric diagnosis.

Cognitive status was assessed with the Mini-Mental State examination (13). Information on demographic

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characteristics, medical diagnoses, and medications was obtained from the nursing records. Diagnoses of dementia, delirium, affective disorder, and schizophrenia were made according to *DSM-III-R*, using the clinical examination, available medical records, and information from family members. Dementia with cerebrovascular disease was diagnosed if there was evidence of a stroke. Dementia with possible Alzheimer's disease was diagnosed if there was a gradual onset of progressive generalized cognitive decline in the absence of other known etiologic factors.

Delusions were diagnosed according to the *DSM-III-R* definition: "a false personal belief based on incorrect inference about external reality and firmly sustained in spite of what almost everyone else believes and in spite of what constitutes incontrovertible and obvious proof or evidence to the contrary" (p. 395). They were subdivided into systematized and nonsystematized delusions according to *DSM-III-R*.

Behavior disturbance before nursing home placement was determined by a structured interview with a family member in which the Psychogeriatric Dependency Rating Scales (14) were used. The behavior problems included physical and verbal aggression, deliberate refusal to obey commands, interfering with activities of others, socially embarrassing behavior (e.g., spitting), noisiness, restlessness, and wandering. Behavior and function in activities of daily living in the nursing home were elicited by an interview with a nursing assistant who also used the Psychogeriatric Dependency Rating Scales. All interviews were performed by trained lay workers or research nurses. The score on the Psychogeriatric Dependency Rating Scales predicts the overall level and type of nursing care required by elderly institutionalized residents, and its validity and interrater reliability have been previously demonstrated (14). The interviews with the patient, family, and nursing staff were conducted independently and within 2 weeks of each other.

Nonparametric statistics were used to compare the characteristics of the delusional and nondelusional groups because the data did not follow a normal distribution. Interval data were tested with the two-tailed Wilcoxon rank-sum test with the standard normal approximation, and nominal data were examined with the chi-square test with Yates' correction by means of the computerized Statistical Package for the Social Sciences (15).

## RESULTS

The demographic characteristics of the sample were similar to those found in a 1981 survey of Maryland nursing homes (1). The mean±SD age of the final sample was 80.5±8.7 years (range=57–108). Ninety-nine (79.2%) of the 125 residents were female, and 116 (92.8%) were white. The psychiatric diagnoses of the sample are shown in table 1. Dementia was seen in 67.2% of the subjects, and overall 84.8% had a psychiatric disorder. The 14 residents in the category "dementia, other causes" contained five cases of dementia associated with major depression, three with metastatic cancer, three with primary brain tumor, two with Parkinson's disease, and one with normal pressure hydrocephalus. The category "other psychiatric disorders" contained nine residents with affective disorders and one with paranoid schizophrenia.

**TABLE 1. Psychiatric Diagnoses of 125 Newly Admitted Residents of Nursing Homes**

| Diagnosis | N | % |
|---|---|---|
| Dementia with possible Alzheimer's disease | 43 | 34.4 |
| Dementia with cerebrovascular disease | 27 | 21.6 |
| Dementia, other causes | 14 | 11.2 |
| Delirium | 12 | 9.6 |
| Other psychiatric disorders | 10 | 8.0 |
| No psychiatric disorder | 19 | 15.2 |

Twenty-six (20.8%) of the residents in the sample were delusional. The delusional residents did not differ significantly from the nondelusional residents in age (mean±SD=79.2±17.2 and 80.8±9.0 years, respectively), race (92.3% and 92.9% white, respectively), and sex (76.9% and 79.8% female, respectively). They did not differ in their need for assistance with activities of daily living. However, delusional residents were more cognitively impaired and showed more behavior problems both at home before admission and in the nursing home after admission (see table 2).

The families reported that behavior problems had led directly to admission in 14 (53.8%) of the delusional cases but only 15 (15.2%) of the nondelusional group ($\chi^2=16.6$, df=1, $p<0.001$). The most common reason for admission in the nondelusional group was that the principal caregiver had become ill. Despite the occurrence of behavior problems and delusions before admission to the nursing home, only six (23.1%) of the delusional residents had seen a psychiatrist in the preceding year. The family recognized delusions before admission in 64% of the cases diagnosed by the psychiatrist as delusional. After admission, nursing assistants identified delusions in only five (19.2%) of the residents who were diagnosed as delusional by the psychiatrist.

The psychiatric diagnoses of the 26 delusional residents varied. All were cognitively impaired. Fifteen had possible Alzheimer's disease, five had dementia due to stroke, two had brain tumors, two had dementia of depression, one was schizophrenic, and one was delirious. Affective disorders were also present in eight of these cases. Besides the two subjects with the dementia syndrome of depression, five others had major depression with mood-congruent delusions and one had a manic syndrome with erotomania.

The delusions of 15 (57.7%) of the residents were systematized, and the delusions of 11 were nonsystematized. Residents with systematized delusions were more cognitively intact than those with nonsystematized delusions (mean±SD scores on the Mini-Mental

**TABLE 2. Scores on Cognitive, Physical Functioning, and Behavior Measures of 125 Delusional and Nondelusional Newly Admitted Residents of Nursing Homes**

| | Delusional Residents (N=26) | | Nondelusional Residents (N=99) | | |
|---|---|---|---|---|---|
| Measure | Mean | SD | Mean | SD | Analysis[a] |
| Mini-Mental State score | 12.8 | 6.3 | 16.9 | 9.7 | Z=−2.39, p<0.02 |
| Psychiatric Dependency Rating Scales | | | | | |
| Activities of daily living score | 12.0 | 8.3 | 13.9 | 9.2 | Z=−0.67, n.s. |
| Behavior subscale score | | | | | |
| Before admission | 6.6 | 4.8 | 3.1 | 4.4 | Z=−3.51, p<0.001 |
| After admission | 5.0 | 4.8 | 2.5 | 3.4 | Z=−3.17, p<0.002 |

[a] Two-tailed Wilcoxon rank-sum test with the standard normal approximation.

State examination were 16.5±4.8 and 7.8±4.8, respectively; Z=−3.52, p<0.001). The systematized delusions took the form of elaborate persecutory beliefs. Nonsystematized delusions were also predominately persecutory, involving theft by unknown persons or by an intruder. Many subjects had delusions in which they misidentified their own or other people's faces (delusions involving prosopagnosia) or did not know where they were (delusional disorientation). An example of the former was a resident who thought her own reflection in the mirror was someone spying on her, and an example of the latter was a resident who claimed she was at a bus station, waiting to go home to her parents.

Fifteen (57.7%) of the 26 delusional residents received daily psychotropic medication. Only one (14.3%) of seven delusional depressed residents received antidepressants. Six (23.1%) of the delusional residents received benzodiazepines for sedation, and another six (23.1%) were taking neuroleptics. Two took lithium carbonate or chloral hydrate.

## DISCUSSION

The sample of nursing home residents we studied resembles other nursing home residents in Maryland (1), so the results may be generalizable. Delusions were diagnosed on the basis of a single clinical examination. Thus, their true prevalence may have been higher than the 20.8% we report, particularly in the severely demented patients, whose delusions may be fleeting and soon forgotten (5, 16). On the other hand, loosely held misinterpretations of everyday events may have been mistaken for delusions in the demented patients. However, an indication of the validity of the study psychiatrist's diagnosis of delusions is provided by the family members' independent reports that delusions occurred before nursing home admission in the majority of cases. The method we used to diagnose possible Alzheimer's disease might have overrepresented this diagnosis because some residents may not have had complete work-ups to exclude other disorders (16), yet the proportion of patients to whom we gave the diagnosis of possible Alzheimer's disease agrees closely with Katzman et al.'s autopsy findings of the prevalence of Alzheimer's disease in nursing home residents (17).

This is the first study to demonstrate that psychiatric disorders (especially dementia), behavior problems, and delusions are present in many nursing home patients before and upon admission. Our findings support the very high prevalence of psychiatric disorder found in previous cross-sectional studies and advances our knowledge by demonstrating that these problems are present at the time of admission rather than occurring as a consequence of long-term nursing home care (18). Chandler and Chandler (3) found a 12% prevalence of delusions in nursing home residents, and Rovner et al. (1) detected a 38% prevalence of delusions and hallucinations in their subjects. Berrios and Brook (5) found that 37% of demented hospital outpatients were delusional, and Cummings et al. (19) described delusions in 30% of outpatients with dementia of the Alzheimer type and 40% with multi-infarct dementia. These results vary because different samples, methods of diagnosing delusions and dementia, and sources of clinical information were used.

We have found that when delusions are present, behavior problems are common. An underlying condition, such as an affective disorder, is infrequently identified and inadequately treated, so, not surprisingly, delusional patients continue to be more behaviorally disturbed than other nursing home residents. Some nursing home placements and behavior problems might be avoided with psychiatric evaluation, diagnosis, and treatment of patients before or soon after admission.

Systematized delusions may respond to specific psychotropic medications. In particular, tricyclic antidepressants alone or in combination with neuroleptics are effective in psychotic depression but were not prescribed for the patients we studied. In contrast, nonsystematized delusions generally do not improve with psychotropic medication because they are usually short-lived and related to cognitive errors. Reassurance and reality orientation by skilled nurses often relieve distress. Unfortunately, we found that in the nursing homes benzodiazepines were quite commonly used to sedate the residents, although benzodiazepines are known to impair cognition (20) and may increase aggression (21).

Traditionally, neurologists manage demented patients, but they have focused less on the noncognitive psychiatric symptoms of dementia. Similarly, nursing home physicians manage medical problems and are often uncertain about treating psychiatric disorders in their demented patients. This is reflected in the rather common use of benzodiazepines to treat delusions and the failure to prescribe antidepressants for major depression. These distinctions are important, because benzodiazepines are largely ineffective and are more likely to impair cognition and increase aggression, and untreated depression is associated with higher mortality rates.

Two measures might improve the recognition of delusions. First, teaching nursing home staff members to recognize delusions and their clinical importance may lead to appropriate referrals to physicians with expertise in geriatric psychiatry. Second, the nursing home staff might ask family members about patients' delusions when they are admitted, since our study shows that families are usually aware of the presence of delusions. While these measures might be helpful for some patients, to improve the quality of care for many more patients, we believe that a broader recognition of the fact that the majority of nursing home patients have unrecognized and untreated psychiatric disorders is necessary.

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# Personality and Emotional Disorder in a Community Sample of Migraine Headache Sufferers

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*To investigate whether individuals who suffer from chronic, severe headaches have more personality abnormalities or emotional disorders than their healthy counterparts, 162 young adults with classical migraine, ascertained by community survey, were compared to matched control subjects without migraine. On the General Health Questionnaire, the prevalence of psychological symptoms among the migraine subjects was 2.5 times the prevalence among the control subjects. The migraine sufferers also had significantly higher scores on the psychoticism (women only), neuroticism, and lie scales of the Eysenck Personality Questionnaire. Frequency of migraine attacks was not related to scores on any of the scales. These results suggest that classical migraine is associated with psychological abnormalities.*

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Patients with the syndrome of classical migraine may experience a variety of psychological alterations during the headache paroxysm as well as in the prodromal period. Changes in sensory (especially visual) functioning, motor abilities, language, memory, mood, and higher-order cognition have been reported to accompany or immediately precede migraine episodes (1, 2). Reports have also indicated that some individuals with migraine have atypical personalities, as well as psychological symptoms and persistent cognitive impairments during headache-free periods (3–5). Chronic migraine sufferers have often been described clinically as ambitious, success oriented, conscientious, perfectionistic, and of above-average intelligence yet tense, rigidly moralistic, and frequently resentful and hostile (2, 6). However, controlled studies have generally failed to reveal consistent psychological profiles of such patients (7).

Andrasik et al. (8), for example, compared migraine patients to patients with muscle contraction headaches, combined migraine and muscle contraction headaches, and cluster headaches on a large battery of personality inventories and symptom rating scales. Quantitative rather than qualitative differences emerged among the groups; the muscle contraction headache group was the most distressed. The migraine group had moderately elevated scores on the hypochondriasis and hysteria scales of the MMPI, but these elevated scores did not distinguish them from the other groups. A study comparing migraine patients to those having combined migraine and muscle contraction headaches (9) found that the latter group had higher scores on the MMPI hypochondriasis, depression, hysteria, and psychasthenia scales. A study by Levor et al. (10) found that migraine sufferers had moderate, subclinical elevations on the MMPI hypochondriasis, depression, and hysteria scales.

Mashayekhi and Berger-Gross (unpublished paper, 1982), noting some of the similarities between migraine and complex partial epilepsy (11–13), studied the behavioral characteristics of unilateral migraine headache and tension headache patients with an instrument developed for the analysis of interictal behavior in epilepsy (14). They found the right unilateral migraine patients to be more obsessional, interpersonally "sticky," angry, and emotional than the tension headache patients, whereas the left unilateral migraine patients were virtually indistinguishable from the tension headache patients. While these findings may be unreliable because of the small group sizes (N=10), they suggest that the role of headache laterality in patients with migraine may be an important variable that has been overlooked in previous studies.

The previous research on personality and psychological disorders in patients with migraine has several additional shortcomings. First, the investigators have relied heavily on the MMPI (15), which may not be the best instrument for the psychological assessment of migraine patients. The MMPI was standardized on samples of psychiatric patients and has a distinct psychopathological bias. It may not be sensitive, therefore, to

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the personality traits found in nonpsychiatric populations generally and headache sufferers specifically. Second, virtually all of the research has used self-selected headache clinic samples rather than epidemiologically defined community samples. Since those who attend specialty clinics may be expected to have headache syndromes that are more severe and/or harder to control, this group may be expected to be more psychologically distressed than the average patient with migraine headaches. In addition, the personality traits of subjects in such clinic samples may be related to the seeking of medical care as well as to the headache syndrome itself (16).

Crisp et al. (17) studied the psychological characteristics of migraine sufferers in the general population of an English market town. They surveyed 1,000 adults and administered interviews about headache symptoms, as well as psychological tests, to 722 eligible individuals. The lifetime prevalence of migraine was found to be 25% in the women and 10% in the men. Using the Middlesex Hospital Questionnaire (18), the authors found that women with migraine reported significantly more anxiety, somatic symptoms, depression, and hysteria than their peers who did not suffer from migraine. Men with and without migraine did not differ significantly on any of the Middlesex Hospital Questionnaire scales.

In one of the few other community-based studies of nonpatients, Ziegler et al. (19) administered the Zung Depression Scale and the Bendig-Taylor short form of the Iowa Manifest Anxiety Scale to 711 community residents. Those with histories of disabling or severe headaches had higher depression and anxiety scores than the comparison groups with mild headache or no headache. This was true for both men and women and in all age ranges. However, subjects whose headaches were characterized by migrainous features (unilateral pain, nausea and vomiting, warning or prodrome) did not differ from those whose headaches were not accompanied by migraine symptoms.

To verify previous reports of greater psychological dysfunction in individuals with the syndrome of classical migraine, we investigated the personalities and psychological distress of subjects with migraine and of matched control subjects, all of whom were randomly selected from the general population. We used the Eysenck Personality Questionnaire (20) to assess the traits of psychoticism (tough-mindedness), neuroticism (emotionality), extraversion, and dissimulation and the 28-item version of the General Health Questionnaire (21) to detect psychological distress of sufficient magnitude to suggest a diagnosable emotional disorder.

## METHOD

A telephone survey of Washington County, Maryland, residents who were 12 to 29 years old and resided in households with telephone service was conducted. This community was selected because of its size (approximately 100,000 inhabitants) and its consistently high participation rates in previous epidemiologic investigations.

The population and survey methods have been described in detail elsewhere (22). In brief, Washington County is located 70 miles northwest of Baltimore, Maryland. Approximately half the population lives in Hagerstown, an urban area and the county seat, while the remaining residents are found in small towns and rural areas. The population is predominantly white. Random-digit dialing was used to identify approximately one-half of the county's 12- to 29-year-old residents. Data were collected by telephone by trained female interviewers, and interviews with 10,169 individuals were completed. The response rate was 94.2%; only 4.3% of the eligible subjects refused. The remaining eligible subjects were not available during the interviewing period (March 1986 to June 1987). These screening interviews ascertained the frequency of headaches, their clinical characteristics and precipitants, and whether treatment for headaches had ever been sought.

A total of 3,723 subjects were called a second time and asked to participate in a longer, more detailed interview on the characteristics, precipitants, and associated features of their headaches (the natural history interview). The criterion for selection for a natural history interview was the subject's report in the screening interview that at least one of the following symptoms had occurred during his or her lifetime: nausea and/or vomiting during a headache; numbness, tingling, or a peculiar feeling in one arm or leg during a headache; unilateral soreness of the scalp accompanying headache; or visual spots, lines, or "heat waves" preceding a headache.

Two groups of subjects were included in the study: individuals with recent histories of frequently occurring migraine headaches (with or without aura) and age- and sex-matched control subjects who had never experienced a migraine headache. The criteria for inclusion in the migraine group were age between 16 and 29 years and meeting the migraine criteria on the natural history interview (see appendix 1). Control subjects were selected from among the individuals between ages 16 and 29 who had completed the screening interview. The criteria for inclusion as a control subject are also shown in appendix 1.

One hundred thirty-one subjects meeting the criteria for the migraine group outlined in appendix 1 were randomly selected for the study. Each subject was mailed a packet of materials that contained a cover letter, a subject data sheet which included a question about laterality of headaches, an informed consent statement, the Eysenck Personality Questionnaire, the 28-item version of the General Health Questionnaire, and a stamped, addressed return envelope. The cover letter began by thanking the recipient for his or her cooperation in the earlier interviews and then introduced the present study on the psychological aspects of migraine and asked for participation. The letter stated that participation was voluntary and that those who completed and returned both questionnaires would be paid $5. Subjects were asked to complete the data sheet and both of the questionnaires and mail them back to the investigators within 2 weeks. Those who did not wish to participate were asked to return all the forms uncompleted. Upon receipt of a set of completed forms, the investigators sent a check for $5 to the subject.

After 3 weeks, subjects who had not responded to the mailing were contacted by telephone and asked to send the forms back either completed or not completed. Three more weeks were allowed for responses. Questionnaires were returned by 93 (71%) of the subjects with migraine. Two sets of questionnaires had missing data, and nine subjects could not be matched to control subjects according to the criteria we have described, leaving 82 migraine subjects. This sample was supplemented by an additional 80 female migraine subjects, all between the ages of 22 and 29, who were participating in a diary-based study of headache precipitants. These subjects had been drawn from the same population by precisely the same sampling methods and with the same selection criteria. They had also completed the General Health Questionnaire and the Eysenck Personality Questionnaire before entering the diary study. These 80 migraine sufferers were combined with the 82 original subjects, resulting in a total of 162 migraine subjects. There were 131 female and 31 male subjects in the migraine group.

For each migraine subject, two potential control subjects were randomly selected from among those who matched the migraine subject in sex, race, age (within 1 year), month in which the screening interview had been administered (within 1 month), and telephone exchange. An assessment package was sent to one of the two potential control subjects. If no response was received within 3 weeks, an assessment package was sent to the second potential control subject. Overall, completed questionnaires were returned by 72% (N=162) of the potential control subjects who received them.

Analysis of variance and paired t tests were used to evaluate the significance of differences in group means. McNemar's test for matched pairs was used to test differences in proportions. Analyses were conducted separately for male and female subjects.

## RESULTS

The characteristics of the migraine and control groups are shown in table 1. There were no significant differences between the groups in education or handedness.

There were highly significant differences between the groups in overall headache frequency. Ninety-three percent (N=151) of the migraine subjects had had at least one headache in the month preceding the interview, compared with 62% (N=100) of the control subjects (McNemar paired $\chi^2=37.31$, df=1, $p<0.0001$). The mean±SD number of headaches reported in the preceding month was substantially higher for the migraine subjects (7.46±7.33) than for the control subjects (3.62±3.54) (paired t=3.87, df=161, $p<0.0002$).

**TABLE 1. Characteristics of Subjects With Migraine and Matched Control Subjects Without Migraine**

| | Migraine Subjects (N=162)[a] | | Control Subjects (N=162)[b] | |
|---|---|---|---|---|
| | N | % | N | % |
| Male sex | 31 | 19.14 | 31 | 19.14 |
| Caucasian race | 162 | 100.00 | 162 | 100.00 |
| Left-handed or ambidextrous | 24 | 14.81 | 22 | 13.58 |
| Education | | | | |
| Did not complete high school | 43 | 26.54 | 35 | 21.60 |
| High school graduate | 62 | 38.27 | 71 | 43.83 |
| At least some college or technical school | 57 | 35.19 | 56 | 34.57 |

[a] Mean±SD age=22.83±4.30 years.
[b] Mean±SD age=22.78±4.28 years.

As shown in table 2, the migraine and control groups varied markedly on the Eysenck Personality Questionnaire. The groups differed dramatically on the neuroticism scale, indicating that the subjects in the migraine group were more tense, anxious, and depressed than those in the control group. The significantly higher psychoticism score of the female migraine group indicates that these women described themselves as less interpersonally sensitive, more hostile, and out of step with their peers. The significantly lower mean score of the migraine subjects on the lie scale suggests that they were less defensive and more willing to admit to discreditable characteristics than were the control subjects.

Group by Sex analyses of variance were performed for scores on each of the Eysenck scales. There were significant sex differences ($p<0.01$) on two variables: psychoticism (men had higher scores) and neuroticism (women had higher scores). There were no significant Group by Sex interactions.

Results on the 28-item General Health Questionnaire indicate significant psychological distress among the migraine subjects (see table 3). The migraine sufferers had higher scores on all of the factor analytically derived symptom scales, as well as higher total scores, than the control subjects. This was true of both male and female subjects. Analyses of variance revealed no main effects of sex nor any Group by Sex interactions.

A total score of 4 to 5 on the General Health Questionnaire has been recommended as the cut-off point for ascertaining cases of emotional disorder (21, 23). In general medical practice settings, this criterion has a sensitivity of 86% and a specificity of 87% (21). If this cut-off score is used, 61.11% (N=99) of the migraine group and 24.69% (N=40) of the control group could be described as having an emotional disorder (McNemar paired $\chi^2=38.67$, df=1, $p<0.001$). (This rate of

**TABLE 2. Scores of 162 Subjects With Migraine and 162 Matched Control Subjects Without Migraine on the Eysenck Personality Questionnaire Scales**

| | Score | | | | | | |
|---|---|---|---|---|---|---|---|
| | Migraine Subjects | | Control Subjects | | | | |
| Scale | Mean | SD | Mean | SD | t | df | p |
| Psychoticism | | | | | | | |
| Men | 4.23 | 2.97 | 3.90 | 2.49 | 0.47 | 30 | n.s. |
| Women | 3.15 | 2.30 | 2.23 | 2.09 | 3.48 | 130 | <0.001 |
| Extroversion | | | | | | | |
| Men | 13.39 | 6.23 | 14.61 | 4.13 | 1.05 | 30 | n.s. |
| Women | 12.74 | 5.59 | 12.28 | 5.21 | 0.64 | 130 | n.s. |
| Neuroticism | | | | | | | |
| Men | 15.23 | 4.73 | 8.45 | 3.86 | 6.16 | 30 | <0.0005 |
| Women | 16.39 | 4.46 | 11.33 | 4.98 | 8.82 | 130 | <0.0005 |
| Lie | | | | | | | |
| Men | 6.87 | 3.07 | 9.26 | 3.91 | 2.96 | 30 | <0.01 |
| Women | 7.99 | 4.31 | 9.47 | 3.96 | 2.78 | 130 | <0.01 |

**TABLE 3. Scores of 162 Subjects With Migraine and 162 Matched Control Subjects Without Migraine on the General Health Questionnaire**

| | Score | | | | | | |
|---|---|---|---|---|---|---|---|
| | Migraine Subjects | | Control Subjects | | | | |
| Scale | Mean | SD | Mean | SD | t | df | p |
| Somatic symptoms | | | | | | | |
| Men | 2.03 | 2.00 | 0.29 | 0.82 | 4.46 | 30 | <0.0005 |
| Women | 1.95 | 1.90 | 0.92 | 1.51 | 5.08 | 130 | <0.0005 |
| Anxiety and insomnia | | | | | | | |
| Men | 2.55 | 2.08 | 0.77 | 1.20 | 4.3 | 30 | <0.0005 |
| Women | 2.78 | 2.30 | 1.10 | 1.68 | 6.96 | 130 | <0.0005 |
| Social dysfunction | | | | | | | |
| Men | 1.26 | 1.15 | 0.29 | 0.78 | 3.61 | 30 | <0.005 |
| Women | 1.42 | 1.65 | 0.70 | 1.15 | 4.03 | 130 | <0.0005 |
| Severe depression | | | | | | | |
| Men | 1.03 | 1.54 | 0.16 | 0.58 | 3.10 | 30 | <0.005 |
| Women | 0.98 | 1.81 | 0.29 | 0.85 | 4.01 | 130 | <0.0005 |
| Total | | | | | | | |
| Men | 6.87 | 4.86 | 1.52 | 1.79 | 5.88 | 30 | <0.0005 |
| Women | 7.14 | 5.58 | 3.02 | 3.88 | 6.99 | 130 | <0.0005 |

psychological disorder among the control subjects approximates that found in other community samples. In a cohort of similar age, sex, and education from the National Institute of Mental Health Epidemiologic Catchment Area survey, 23.42% had "positive" scores on a 20-item General Health Questionnaire [G. Nestadt, personal communication, September 1988].)

Within the entire migraine group, there were no significant correlations between scores on any of the Eysenck scales or the General Health Questionnaire scales and frequency of headaches (number in the past month and number in the past year). When male and female subjects were considered separately, the same results were obtained.

Of the 162 migraine subjects, 144 answered the question on laterality of headache. Four reported always having left-side headaches, 25 usually had their headaches on the left, two reported exclusively right-side headaches, 50 usually had right-side headaches, 43 reported that they had right-side and left-side headaches with equal frequency, and 20 reported never having lateralized pain (although having lateralized pain had been a criterion for inclusion in the migraine group). Analyses of variance revealed no significant differences among the various laterality groups on any of the General Health Questionnaire symptom scales (or the total score) or on the Eysenck Personality Questionnaire scales.

The contribution of coexisting medical disorders to the personality characteristics and emotional distress of the migraine sufferers was also examined. The migraine group was divided into those who had and those who did not have a number of medical conditions (hypertension, mitral valve prolapse, irregular heart beat, epilepsy, Raynaud's syndrome, hay fever, asthma, eczema, fainting spells, brain surgery or radiation treatment, meningitis or brain infection, and concussion). In none of these comparisons was there a difference between those with and those without the disorder on the General Health Questionnaire total score or on any of the Eysenck Personality Questionnaire scales.

## DISCUSSION

In this case-control, questionnaire-based study of community residents, individuals with migraine headaches were shown to differ in significant ways from those without migraine headaches. Women with migraine had elevated scores on the neuroticism and psychoticism scales of the Eysenck Personality Questionnaire and lower scores on the lie scale. Their modal personality could therefore be described as unguarded, anxiety prone, depressive, lacking in interpersonal warmth, and somewhat alienated from peers. The fewer male migraine subjects were similar, although they were no more alienated, insensitive, or tough-minded than their nonmigraine counterparts. The migraine sufferers of both sexes had significantly higher scores on the General Health Questionnaire. They were more likely to suffer from substantial psychological symptoms, including anxiety, depression, and impaired social functioning. Sixty-one percent of the migraine group was sufficiently distressed to warrant further evaluation and possibly treatment. This prevalence was 2.5 times higher than that found in the nonmigraine control subjects.

Unlike some previous studies, this study found no major differences between men and women in the extent to which the presence of migraine influenced psychological functioning. Crisp et al. (17) reported a nonsignificant tendency for male migraine subjects to be more anxious and less phobic and to have more somatic symptoms than men without migraine. Differences in diagnostic criteria, assessment instruments (Middlesex Hospital Questionnaire versus the Eysenck Personality Questionnaire and the General Health Questionnaire), and cultures (English versus American) may have contributed to the conflicting findings in Crisp et al.'s study and our study. Our study also failed to find personality or emotional differences attributable to headache laterality or related to the presence of coexisting medical disorders.

The absence of a significant relationship between headache frequency and severity of psychological distress or personality abnormality is surprising. Ziegler et al. (19) found that higher frequency of headaches was strongly associated with a higher self-rating of depression among both men and women with severe headaches in a community sample. The same was true, to a somewhat lesser extent, of self-reported anxiety. The lack of a relationship between Eysenck and General Health Questionnaire variables and headache frequency in the present study may suggest that it is not the headache events themselves that are responsible for the psychological difficulties of migraine sufferers. It is possible that individuals who report having headaches with migrainous features are simply more willing to report a variety of psychological symptoms. The fact that the migraine group had a lower score on the Eysenck lie scale supports the hypothesis that these subjects were less defensive and more self-critical. Their responses may also suggest a certain degree of hypervigilance and perfectionism, in which ordinary somatic and psychological experiences are interpreted as symptoms of disorder. Bond (24) reported that female cancer patients who complained vigorously of pain tended to have higher neuroticism and extroversion scores on the Eysenck Personality Inventory. Similarly, Philips and Jahanshahi (25) found that scores on the neuroticism and extroversion scales, but not on the lie scale, were positively correlated with reported magnitude of pain in a large clinic sample of headache sufferers.

Many patients with frequent, severe headaches have clinically significant depression. The present study found indications of serious depression among migraine subjects identified in a community survey. In this regard, it is noteworthy that tricyclic antidepressants are often effective in reducing the frequency and severity of migraine headaches (26), even in patients without clinically obvious depression (27).

The absence of a relationship between headache frequency and personality traits or psychological symptoms suggests that having frequent, severe headaches is not itself the cause of psychological difficulties. Common etiological factors may underlie both migraine headaches and anxious, depressed, socially alienated dispositions. Several lines of investigation, including research on the efficacy of tricyclics, suggest a common biological mechanism. Recent evidence that the migraine syndrome itself may be a primary neurologic disorder with secondary vasomotor symptoms (28–30) raises the possibility that at least some of the psychological features are direct results of cerebral pathology or dysfunction (31). The report by Hooker and Raskin (5) that patients with common or classical migraine displayed cognitive deficits on a neuropsychological test battery supports the conjecture of an interictal disturbance in cerebral function.

Among the shortcomings of the present study is that a group of subjects with frequent, severe headaches without migrainous features was not included for comparison. It is therefore impossible to say whether the psychological features observed in our migraine group are shared by chronic tension headache sufferers. Studies by Andrasik et al. (8), Philips and Jahanshahi (25), and Philips (32) suggest that there are quantitative rather than qualitative differences between the psychological experiences of pain in tension headache and migraine headache patients.

The General Health Questionnaire and the Eysenck Personality Questionnaire provided us with empirical evidence that migraine sufferers in the community are different psychologically from individuals who do not have migraine, but they do not provide information for making psychiatric diagnoses. Future studies might use clinical psychiatric examinations (including, if possible, information provided by an informant) to produce diagnostic information on the emotional and personality vulnerabilities of migraine sufferers.

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## APPENDIX 1. Criteria for Inclusion in Study on Migraine Headache Sufferers

MIGRAINE GROUP (based on natural history interview)

1. Subject answers yes to both of the following:
   Have you ever had nausea or been sick to your stomach during a headache but not because of a cold or the flu?
   Have you ever had headache pain mostly on one side of your head?
2. Subject answers yes to at least one of the following:
   Have you ever had numbness, tingling, a peculiar feeling, or a definite weakness in one arm or leg during a headache?
   Have you ever had numbness, tingling, a peculiar feeling, or a definite weakness in one arm or leg before a headache?
   Have you ever seen spots, lines, or "heat waves" in one or both eyes before a headache?
   Have you ever had partial loss of sight to the right or left side of vision before a headache?
3. Subject had at least two headaches in the past month.

CONTROL GROUP (based on screening interview)

1. Subject answers no to all of the following:
   Have you ever had nausea or been sick to your stomach during a headache but not because of a cold or the flu?
   Have you ever had numbness, tingling, a peculiar feeling, or a definite weakness in one arm or leg during a headache?
   Have you ever seen spots, lines, or "heat waves" affecting one or both eyes before a headache?
   Have you ever had partial loss of sight to the right or left side of vision before a headache?
   Have you ever had soreness of the skin or skin sensitive to touch on only one side of the head during a headache?

# Greater Left Cerebral Hemispheric Metabolism in Bulimia Assessed by Positron Emission Tomography

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*Eight women with bulimia and eight age- and sex-matched normal control subjects were studied with positron emission tomography using [$^{18}$F]-fluorodeoxyglucose (FDG) as a tracer of brain metabolic rate. Subjects performed a visual vigilance task during FDG uptake. In control subjects, the metabolic rate was higher in the right hemisphere than in the left, but patients with bulimia did not have this normal asymmetry. Lower metabolic rates in the basal ganglia, found in studies of depressed subjects, and higher rates in the basal ganglia, reported in a study of anorexia nervosa, were not found. This is consistent with the suggestion that bulimia is a diagnostic grouping distinct from these disorders.*

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Bulimia nervosa is a psychiatric illness seen primarily in young adult women, characterized by episodic binge eating and purging and preoccupation with body image. Unlike patients with anorexia nervosa, who lose more than 15% of their ideal body weight through restricting caloric intake, bulimic patients maintain a relatively normal body weight. The cognitive patterns of the two groups are similar, but their eating behavior and body weights differ. The etiology of bulimia nervosa is uncertain and may involve endocrine (1–3), neurochemical (4–8), genetic (2, 5), and sociocultural factors. Some studies have suggested neuroanatomical abnormalities in patients with bulimia nervosa on the basis of CT scan (9, 10); however, there are no reports of functional brain metabolism in patients with bulimia without a co-diagnosis of anorexia.

Krieg et al. (9) compared the CT scans of normal-weight bulimic patients with those of anorexic patients and normal control subjects. They found that both groups of patients with eating disorders showed ventricular enlargement and sulcal widening. These results suggest that morphological brain alterations may be a consequence of endocrine and metabolic reactions to starvation, regardless of whether starvation leads to an underweight state. Bulimic patients maintain a normal weight through binge eating and purging and often restrict caloric intake between binges, inducing a brief starvation-like state. Therefore, if anorexia nervosa and bulimia share common anatomical changes on CT scan, it is possible that they might also have similarities in functional brain metabolism as assessed by positron emission tomography (PET) scan.

Brain imaging studies of cerebral metabolism have not been reported previously for normal-weight bulimic patients. However, several papers have been published on a sample of seven women with anorexia nervosa, four of whom also reported bulimic symptoms of binge eating and vomiting (11–13). The subjects, who were 25%–40% below ideal body weight at the time of the first PET scan and 10%–19% below ideal body weight for the second, were compared with a control group of 15 normal men. Significant hypermetabolism of the caudate bilaterally, as well as significant cortical hypermetabolism, was present in the anorexic state; these normalized with weight gain.

To address the possibility of abnormalities of functional brain metabolism in bulimia nervosa while avoiding the possible artifacts of concurrent starvation, we studied eight female patients with bulimia nervosa and eight normal women of the same age.

## METHOD

### Subjects

Eight female patients with bulimia and eight age- and sex-matched normal control subjects served as subjects. The mean±SD age of the patients was 28.6±6.5 years, six were right-handed and two were left-handed, their mean height was 64.9±3.6 inches, their mean weight was 133.6±16.9 lb, and their mean percent of ideal body weight was 107.6%±10.1%. The mean age of the control subjects was 28.9±7.7

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years, all were right-handed, their mean height was 65.1±2.4 inches, their mean weight was 127.4±13.6 lb, and their mean percent of ideal body weight was 102.5%±8.2%. All bulimic patients received psychiatric interviews and met *DSM-III-R* criteria for bulimia. None had an earlier history of anorexia.

The patients were evaluated with the Eating Attitudes Test (14), the 21-item Hamilton Rating Scale for Depression, and a count of the number of episodes per week of vomiting and binge eating. Their mean Eating Attitudes Test score was 37.8±10.3, and their mean Hamilton depression score was 20.8±6.9. They had a mean±SD of 14.1±10.0 binge episodes per week and vomited 14.3±9.2 times a week.

All subjects had been free of all psychoactive medications for a minimum of 30 days. They were in good physical health and none had significant abnormalities on physical examination or laboratory screening tests. Subjects with a history of seizure disorders, major head trauma, or current substance abuse were excluded.

All patients and control subjects provided informed consent to participation in the study.

### *Image Collection and Analysis*

All subjects performed the Continuous Performance Test (15) while sitting in a soundproof, darkened room during the uptake of [$^{18}$F]-fluorodeoxyglucose (FDG), as described elsewhere (16), except that they performed the test without continuous feedback.

Subjects had a previously custom-formed thermoplastic mask placed on their heads to prevent head movement during the hour-long scanning procedure. Nine planes were obtained parallel to the canthomeatal line at 10-mm increments starting at 95 mm. The in-plane resolution of the PET scanner was 7.6 mm and the axial resolution was 9.9 mm.

Three slices for analysis were chosen by a rater without knowledge of diagnosis to match the appearance to a standard photographic atlas (17). For each slice (18) the cortical region was outlined as described elsewhere (16, 18) and divided into four anteroposterior sectors. An index of hypofrontality was calculated as the ratio of anterior sector 1 to posterior sector 4. This was done for the right and left side separately and for the sum of the right and left sides. A ratio over 1.0 thus indicated frontal metabolic rate greater than posterior metabolic rate.

The image from the atlas (17) was digitized, and the proportional locations of boxes identified on the digitized atlas on the anteroposterior and lateral directions were then transferred automatically to the PET slices (16). Mean glucose metabolic rates were then calculated for the left- and right-sided boxes (right side as mirror image of left around the vertical meridian). Values of glucose use in micromoles of glucose/100 g of brain per minute were calculated according to the model of Sokoloff et al. (19) by using our adaptation (16) of a program developed by Sokoloff and constants from Phelps et al. (20). All subjects had plasma glucose values within normal limits during uptake and scanning. For each area of interest, the value was expressed as mean glucose use (the sum of pixel values divided by the number of pixels contained in the area). Data were analyzed as expressed in units of micromoles of glucose/100 g of brain per minute and also as ratios to whole-slice glucose metabolic rate. Analysis based on absolute glucose metabolic rate provides valuable information on the degree of actual neural activity. However, analysis with ratios of metabolic rates allows for the normalization of absolute baseline differences, which can otherwise obscure relative regional differences in brain metabolism.

Glucose data were analyzed by using repeated measures analysis of variance (ANOVA) (21). This approach was chosen because the multiple determinations of metabolic rate within each subject were arranged in discrete dimensions (e.g., right and left hemisphere). Since cortical sectors were arranged in a contiguous sequence, both horizontally and vertically, trend analysis was also used to test for anteroposterior or top/bottom (dorsal/ventral) gradients. The Huyhn-Feldt correction for degrees of freedom was used throughout.

## RESULTS

### *Cortical Surface*

Normal women showed relatively higher metabolic rates in the right hemisphere. In contrast, women with bulimia lost this normal asymmetry; their metabolic rates were similar in both hemispheres (see table 1). This pattern was confirmed statistically with a four-way ANOVA with independent groups (patients and control subjects) and repeated measures for anteroposterior position (sectors 1 through 4), hemisphere (left and right), and level (supra-, mid-, and infraventricular) (see table 1), which remained significant when the two left-handed subjects were omitted. The absolute metabolic rate data did not yield a significant group effect or group interaction.

The largest difference between patients and normal subjects was in the right posterior sector, which includes the right parietal and right temporal lobes. Here, bulimic patients had high absolute and high relative metabolic rates on the left in contrast to the higher rates on the right in normal subjects. This was confirmed by t tests on left minus right differences (see table 1).

### *Subcortical Structures*

We examined the metabolic rate in the caudate nucleus first because Herholz et al. (11) observed higher relative metabolic rates in bulimic patients than normal subjects. We found no significant difference in either absolute or relative metabolic rates (for 41% head

**TABLE 1. Brain Metabolic Rates of Women With Bulimia and Age- and Sex-Matched Normal Control Subjects**

| | Bulimic Subjects (N=8) | | Control Subjects (N=8) | |
|---|---|---|---|---|
| Item | Left | Right | Left | Right |
| Relative cortical metabolic rate (region/whole slice)[a] | | | | |
| Anterior | 1.07 | 1.08 | 1.09 | 1.11 |
| Mid-anterior | 1.07 | 1.10 | 1.05 | 1.11 |
| Mid-posterior | 1.02 | 1.00 | 0.99 | 1.05[b] |
| Posterior | 1.05 | 1.08 | 1.03 | 1.06 |
| Absolute subcortical metabolic rate (μmol/100 g brain per minute)[c] | | | | |
| Combined 41% head height | 20.86 | 21.37 | 20.73 | 23.77 |
| 28% head height | | | | |
| Cingulate | 20.63 | 19.20 | 20.80 | 23.03[d] |
| Ventral caudate | 18.33 | 19.63 | 18.68 | 20.13 |
| Ventral putamen | 20.87 | 19.10 | 19.95 | 22.05[e] |
| Basal forebrain | 13.23 | 13.20 | 15.40 | 13.60 |
| Midbrain | 14.23 | 13.97 | 11.03 | 10.75 |
| Combined | 17.46 | 17.02 | 17.17 | 17.91 |
| Relative subcortical metabolic rate (region/whole slice)[f] | | | | |
| Combined 41% head height | 1.11 | 1.14 | 1.06 | 1.21 |
| Combined 28% head height | 1.01 | 1.03 | 1.03 | 1.08 |

[a] Significant Hemisphere by Sector by Group interaction (F=2.98, df=3, 36, p=0.05).

[b] Significant difference between bulimic patients and control subjects in left−right differences (t=2.4, df=7, p<0.05).

[c] Significant Hemisphere by Group interactions (41% head height: F=5.62, df=1, 12, p=0.035); 28% head height: F=4.65, df=1, 12, p=0.05). Significant Hemisphere by Structure by Group interaction (F=4.48, df=1, 12, p=0.038).

[d] Significant difference between bulimic patients and control subjects in left−right differences (t=2.5, df=7, p<0.05).

[e] Significant difference between bulimic patients and control subjects in left−right differences (t=2.4, df=7, p<0.05).

[f] Significant Hemisphere by Group interactions (41% head height: F=4.90, df=1, 12, p=0.047; 28% head height: F=5.63, df=1, 12, p=0.04).

height, the value for the normal subjects on the right was 23.80, for the bulimic patients it was 26.40, p>0.10).

Next, exploratory analyses were carried out on regions of interest from two levels: 41% and 28%. For each slice level, five regions were selected (caudate, putamen, anterior thalamus, medial thalamus, and posterior thalamus for the 41% slice and cingulate, ventral caudate, ventral putamen, basal forebrain, and midbrain for the 28% slice). Measurements were obtained in both hemispheres. A four-way ANOVA, similar to the one used in the analysis of the cortical surface, was used; post hoc t tests on left minus right differences were used to follow up the observed Group by Hemisphere interactions.

In the basal ganglia and thalamus, high absolute and relative metabolic rates were seen on the right (see table 1). Patients with bulimia showed less right lateralization than control subjects for the 41% and 28% slices for both absolute and relative metabolic data.

## DISCUSSION

This study presents the first investigation of brain metabolism in normal-weight patients with bulimia nervosa. The left hemisphere activity of bulimic patients was higher and the right hemisphere activity of bulimic patients was lower than those of normal control subjects. For specific brain regions, the right parietal/temporal region (hemispheric sector 3) as well as parts of the medial frontal lobe, thalamus, and putamen appeared to show this reversal of the normal right-greater-than-left pattern. Although two of our eight bulimic patients were left-handed, the significant Hemisphere by Group interactions were present even when the two left-handers were excluded from the ANOVA. It is important to keep in mind the small sample size of this study and the necessity for replication with a larger sample. This finding of abnormal hemispheric lateralization is seen best with the metabolic ratio analysis, which is more sensitive to relative differences between different brain regions because of the normalization for nonspecific global differences.

The only other PET study in the current literature on eating disorders includes women with the diagnosis of anorexia nervosa, some of whom had symptoms of bulimia (11). We were unable to find the higher metabolic rates in the caudate and temporal lobes bilaterally reported in that study. This suggests the possibility that there is a neurobiological difference between bulimia and anorexia nervosa.

Patients with bulimia did not exhibit the lower relative caudate activity found in depression (22, 23), nor did these earlier depression studies find a significant left-versus-right asymmetry differentiating normal and affectively ill groups. This suggests that patterns of brain metabolism in women with bulimia nervosa differ from those observed in major affective disorders.

Our results seem unlikely to be artifacts of cerebral metabolic effects of starvation or head position. All of our patients were within 10% of their ideal body weight and had been eating normally on the day before the scan; no patient had an abnormal plasma glucose value. The finding of a left-greater-than-right asymmetry in the cortex across several planes tends to militate against the explanation of a lateral head tilt, since broad areas of the cortex would be relatively insensitive to small lateral head tilt.

The loss of right-greater-than-left temporal lobe asymmetry in bulimic patients raises questions about the possible role of lack of hemispheric lateralization in the etiology of this disorder. Hemispheric lateralization in affective function has been proposed, but little has been written about the possible role of lateralization in eating behavior. Mayberg et al. (24) found that lateralized change in brain function due to stroke damage had differential effects on mood and serotonin receptor density as assessed by PET scans. The differential change in serotonin system as a response to lateralized damage has some implications for bulimia, in which the serotonin system has been hypothesized to be involved.

In summary, our findings suggest that women with bulimia nervosa have some specific metabolic brain abnormalities when compared with normal women, anorexic patients, and depressed patients. This suggests that bulimia nervosa represents a distinctive psychiatric illness. One limitation of our study was the small sample size. Future studies with larger samples are necessary.

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# A Community Study of Anxiety in Children and Adolescents

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*The authors used an epidemiologic approach to investigate rates, symptoms, and behavioral concomitants of anxiety across the child and adolescent age span. They drew 210 children aged 8, 12, and 17 in equal numbers from a community sample and evaluated them with structured diagnostic assessments. They found anxiety to be the most frequently reported type of psychopathology across all three age groups. Although the prevalence of any anxiety symptom remained constant, specific types of anxiety varied with age. Age differences in nonanxiety behavior were found between subjects with and without anxiety, particularly with regard to interpersonal dysfunction.*

(Am J Psychiatry 1990; 147:313–318)

The role of anxiety has been considered central to the understanding of the entire range of childhood psychopathology. Anxiety has clinical importance not only as a distinct set of disorders but also because it exerts an effect on other domains of functioning. Additionally, anxiety would appear to influence other disorders indirectly: many thought processes as well as behavioral and physiological responses may be dramatically altered under the influence of anxiety (1). Given its clinical importance, examination of the developmental progression of anxiety should be a research priority. However, until recently the study of anxiety in children and adolescents has been limited to descriptions of symptoms such as fears or phobias (2, 3).

During the past several years the literature pertaining to anxiety and children has increased, including reports on children whose parents have anxiety disorders (4, 5) and studies of clinically referred children with anxiety (6–10). Regarding the latter, Last et al. (6) warned that findings in clinically referred children with anxiety disorders may not be applicable to the general population of children with anxiety. Because many children in the general population are neither referred nor treated, study of a representative community sample can provide a nonbiased database on anxiety symptoms in children and adolescents. Adding a developmental perspective to the epidemiologic approach would provide even more useful information on this type of psychopathology, particularly with regard to quantitative versus qualitative differences and continuities and discontinuities across ages (11).

We recently reported rates of anxiety disorders and their associated characteristics in a community sample of mid-adolescent subjects (12). The current cross-sectional study provides data across a broader age group of children and adolescents with a focus on comparisons across ages. The objective of this paper is threefold: first, to examine rates and symptoms of anxiety across the age span; second, to compare patterns of nonanxiety behavior in anxious and nonanxious subjects across ages; third, to explore characteristics that differentiate anxious and nonanxious subjects at three age levels.

## METHOD

### *Subjects and Procedure*

The sample consisted of 210 subjects chosen from a public school list of 4,810 children (1,745 8-year-olds, 1,578 12-year-olds, and 1,487 17-year-olds). (There is no private school in this city.) The subjects were selected by a stratified random method based on age (8, 12, and 17 years old) and by sex (105 boys and 105 girls), and every *i*th name was drawn. The sample size was determined by the financial restraint established by the granting agency. According to Hollingshead and Redlich's social class index (13), 42 (20.0%) of the 210 students were in class I, 73 (34.8%) in class II, 57 (27.1%) in class III, 35 (16.7%) in class IV, and three (1.4%) in class V. In regard to racial composition, 187 (89.0%) of the students were Caucasian, 19 (9.0%) were black, and four (1.9%) were Oriental or other. (The catchment area was 90% Caucasian, 8% black, 1% Oriental, and 1% Hispanic.)

Of 377 families originally contacted, 289 (76.7%) agreed to participate; no information was available on the families who refused. We stopped interviewing when we reached the desired number of subjects from each age group and of each gender. The prospective

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**TABLE 1. Prevalence of Anxiety in 210 Children and Adolescents**

| | 8-Year-Olds (N=70) | | 12-Year-Olds (N=70) | | 17-Year-Olds (N=70) | | Boys (N=105) | | Girls (N=105) | | Total (N=210) | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Type of Anxiety | N | % | N | % | N | % | N | % | N | % | N | % |
| Separation anxiety disorder | 13 | 18.6 | 6 | 8.6 | 8 | 11.4 | 5 | 4.8 | 22 | 21.0 | 27 | 12.9 |
| Overanxious disorder | 6 | 8.6 | 8 | 11.4 | 12 | 17.1 | 10 | 9.5 | 16 | 15.2 | 26 | 12.4 |
| Simple phobia | 2 | 2.9 | 2 | 2.9 | 3 | 4.3 | 1 | 1.0 | 6 | 5.7 | 7 | 3.3 |
| Social phobia | 0 | 0.0 | 1 | 1.4 | 1 | 1.4 | 1 | 1.0 | 1 | 1.0 | 2 | 1.0 |
| Any anxiety | 18 | 25.7 | 11 | 15.7 | 15 | 21.4 | 14 | 13.3 | 30 | 28.6 | 44 | 21.0 |

subjects were approached by telephone; the caller explained the project and offered $50 per child as an incentive for participation. (The U.S. census indicates that about 4% of the households in this community would not have a telephone.) After the family agreed to participate, an appointment was made to conduct the interviews in the subject's home. Both the child and the child's mother were interviewed by structured interview (the Child Assessment Schedule and the Parents' Child Assessment Schedule) (14, 15); additionally, the child completed an anxiety self-report form.

All participating children and their parents provided informed consent to participation in the study after its nature had been explained to them.

### *Interviewers' Training*

The interviewers' training was conducted by D.J. Burbach, who collaborated with K.K. Hodges (15; unpublished 1985 paper). The interviewers were doctoral students in psychology or child and family development who had previous experience working with children. Training included extensive review of relevant material (such as the Child Assessment Schedule manual), role playing, and rating and discussing videotaped Child Assessment Schedule interviews. In addition, the interrater reliability was assessed. These procedures were based on the recommendations of Hodges and Burbach (unpublished 1985 paper), who were involved in their implementation.

During the role play, all interviewers met an initial item-by-item kappa criterion of 0.80. The interrater reliability was formally evaluated by requiring interviewers to rate videotaped Child Assessment Schedule interviews administered to clinically referred children. This procedure yielded a mean±SD kappa of 0.92± 0.02 (range=0.89 to 0.96). During the course of data collection, interviewers were continually monitored to minimize interviewer's drift (16).

### *Instruments*

*Child Assessment Schedule.* The Child Assessment Schedule is a semistructured diagnostic interview designed to assess child and adolescent psychopathology. A parallel form, the Parents' Child Assessment Schedule, is administered to parents about their children. Reliability and validity data on these interviews have been previously reported (14, 15). These instruments allow for the determination of *DSM-III* diagnoses. In addition, the Child Assessment Schedule assesses various areas of adjustment and functioning. Scores are then derived by summing the items in several broad areas of functioning (e.g., school, family, self-image). Symptoms relevant to a specific diagnosis can also be totaled into symptom complex scales to provide a more detailed picture of specific categories of behavior. High scores on these scales are indicative of greater difficulty.

*Revised Children's Manifest Anxiety Scale.* The Revised Children's Manifest Anxiety Scale was developed by Reynolds and Richmond (17) to assess chronic manifest anxiety in children and adolescents. It yields subscale scores in three areas of anxiety: physiological, oversensitive, and concentration. Higher scores on these subscales reflect greater anxiety. The Revised Children's Manifest Anxiety Scale has a high degree of concurrent validity when compared with the trait measure on the State-Trait Anxiety Inventory for Children (18).

### *Statistical Analyses*

Frequency data for the three groups were compared by using chi-square analyses. To compare differences in medians between two and among three groups, we used Wilcoxon and Kruskal-Wallis analyses of ranks, respectively. All tests of significance used two-tailed p values. Specific group differences were examined by using post hoc nonparametric group comparison methods. Although some might think that use of a Bonferroni-corrected p value would be more appropriate than an uncorrected p value, we felt that this was too conservative for an exploratory study and therefore did not use a Bonferroni correction.

## RESULTS

We examined several aspects of anxiety. First, we examined the frequencies of and relationships among categories of anxiety. Second, we examined frequencies of specific symptoms of anxiety across age groups. Third, we explored the differences between anxious and nonanxious children in the three age groups in the frequency of nonanxiety symptoms. Finally, we compared anxious and nonanxious children in each age category.

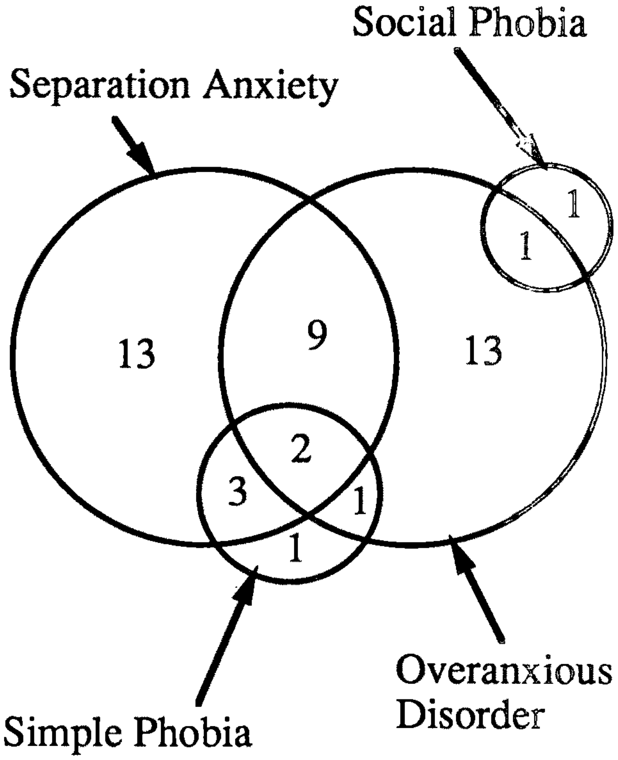
Forty-four (21.0%) of the 210 children had anxiety according to the Child Assessment Schedule, and 29 (13.8%) had anxiety according to the Parents' Child Assessment Schedule. Anxiety was the most frequently reported type of psychopathology in this community sample. The kappa coefficient reflecting the agreement between parent and child was 0.16, indicating that agreement between parent and child concerning anxiety was poor. Only 10 (4.8%) (six girls and four boys) of the children were found to have anxiety according to both the Child Assessment Schedule and the Parents' Child Assessment Schedule.

Children were diagnosed as having anxiety if they met the algorithm of the Child Assessment Schedule Manual (or the Parents' Child Assessment Schedule) specifically for anxiety based on *DSM-III* criteria for separation anxiety disorder, overanxious disorder, avoidant disorder, simple phobia, and social phobia. Table 1 provides the Child Assessment Schedule rates of specific types of anxiety for boys and girls and for 8-, 12-, and 17-year-olds. According to these data, the 8-year-olds had higher rates of separation anxiety disorder but the 17-year-olds had higher rates of overanxious disorder; the three groups had similar rates of phobic disorders. Girls reported significantly more anxiety than boys ($\chi^2=7.13$, df=1, $p<0.01$), which is consistent with data reported in the adult literature (19). Data from parents' interviews showed similar patterns, except that all the reported rates were lower. This also is consistent with data from other investigators, who found that parents reported lower rates of internalizing disorders in their children than children reported in themselves (20). An examination of socioeconomic status and race and anxiety provided no significant associations.

The degree of overlap in the prevalence of specific types of anxiety is depicted in figure 1. Sixteen (36.4%) of the 44 children with anxiety met criteria for two or more anxiety diagnoses. The possible explanations for this finding include 1) the presence of one type of anxiety acts as a risk factor for others, 2) different types of anxiety have the same etiology or nonspecific risk factors, and 3) the symptoms of various types of anxiety overlap and result in subjects meeting criteria for more than one diagnosis.

Due to the small sample size and the low frequencies of specific disorders, we reserved the statistical examination of differences between the age groups to symptom clusters, thereby also minimizing the effects of diagnostic errors by structured interviews. As shown in table 2, fear of separation was significantly less prevalent and social fears were significantly more prevalent among the 12- and 17-year-olds. Symptoms characteristic of overanxious disorder (i.e., anxiety about past imperfections) were also more prevalent among the 17-year-olds. Data from parent interviews showed similar patterns with regard to age groups and types of anxiety. Scores on the Revised Children's Manifest Anxiety Scale showed that the 12- and 17-year-olds had significantly lower rates of physiological symptoms and significantly higher rates of social anxiety than the 8-year-olds; the 17-year-olds also had significantly higher rates of worry items than 12- or 8-year-olds (see table 2).

**FIGURE 1. Overlap of the Types of Anxiety in 44 Adolescents and Children**[a]



[a]The numbers in each area represent the numbers of children and adolescents.

Using Wilcoxon tests with normal approximations, we compared the scores on three Revised Children's Manifest Anxiety Scale subscales by diagnostic status. The 44 anxious subjects had significantly higher physiological subscale scores ($Z=4.09$, $p<0.0001$), higher oversensitive subscale scores ($Z=3.08$, $p<0.002$), and higher concentration subscale scores ($Z=2.59$, $p<0.01$) than the 166 nonanxious subjects.

Table 3 shows the patterns of nonanxiety symptoms in anxious and nonanxious subjects for the three age groups. For the psychopathology symptom complexes (depression, acting out, conduct), anxious and nonanxious subjects showed similar frequency patterns across age groups, although the anxious subjects had consistently higher scores on these scales. However, data for the symptom complexes involving friends and family showed different patterns. Problems with friends, although consistently high in all three age groups of anxious subjects, were significantly less prevalent among nonanxious 17-year-olds and 12-year-olds than among nonanxious 8-year-olds. On the

**TABLE 2. Prevalence of Anxiety Symptoms From the Child Assessment Schedule and the Revised Children's Manifest Anxiety Scale in 8-, 12-, and 17-Year-Olds[a]**

| Instrument and Symptom | 8-Year-Olds (N=70) | | 12-Year-Olds (N=70) | | 17-Year-Olds (N=70) | | $\chi^2$ (df=2) | p |
|---|---|---|---|---|---|---|---|---|
| | N | % | N | % | N | % | | |
| Child Assessment Schedule | | | | | | | | |
| Fear of separation[b] | 36 | 51.4 | 23 | 32.9 | 11 | 15.7 | 20.1 | <0.001 |
| Fear of strangers[c] | 28 | 40.0 | 13 | 18.6 | 13 | 18.6 | 11.2 | <0.004 |
| Anxiety about past imperfections[d] | 6 | 8.6 | 7 | 10.0 | 23 | 32.9 | 18.3 | <0.001 |
| Fear of social situations[c] | 15 | 21.4 | 32 | 45.7 | 39 | 55.7 | 18.0 | <0.001 |
| Revised Children's Manifest Anxiety Scale | | | | | | | | |
| Often feel sick to stomach[b] | 25 | 35.7 | 13 | 18.6 | 8 | 11.4 | 12.7 | <0.002 |
| Have bad dreams[c] | 26 | 37.1 | 7 | 10.0 | 10 | 14.3 | 18.8 | <0.001 |
| Worry a lot[d] | 20 | 28.6 | 18 | 25.7 | 39 | 55.7 | 16.3 | <0.001 |
| Worry what others think of me[c] | 27 | 38.6 | 47 | 67.1 | 47 | 67.1 | 14.9 | <0.001 |

[a] Similar trends were found for symptoms on the Parents' Child Assessment Schedule.

[b] 8-year-olds were significantly different from 12-year-olds and 17-year-olds; 12-year-olds were significantly different from 17-year-olds ($p<0.05$, chi-square).

[c] 8-year-olds were significantly different from 12-year-olds and 17-year-olds ($p<0.05$, chi-square).

[d] 8-year-olds and 12-year-olds were significantly different from 17-year-olds ($p<0.05$, chi-square).

**TABLE 3. Nonanxiety Symptoms on the Child Assessment Schedule of Three Age Groups of Anxious and Nonanxious Children and Adolescents**

| Symptom | 8-Year-Olds | | | 12-Year-Olds | | | 17-Year-Olds | | | $\chi^2$ (df=2) | p |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Score | | | Score | | | Score | | | |
| | N | Mean | SD | N | Mean | SD | N | Mean | SD | | |
| Depression | | | | | | | | | | | |
| Anxious subjects | 18 | 7.1 | 5.8 | 11 | 8.6 | 3.6 | 15 | 9.5 | 4.2 | 3.0 | n.s. |
| Nonanxious subjects[a] | 52 | 3.9 | 2.7 | 59 | 4.2 | 3.6 | 55 | 5.3 | 3.0 | 8.4 | <0.02 |
| Acting out | | | | | | | | | | | |
| Anxious subjects | 18 | 8.5 | 4.0 | 11 | 7.7 | 2.8 | 15 | 11.2 | 5.5 | 3.7 | n.s. |
| Nonanxious subjects[a] | 52 | 5.0 | 2.8 | 59 | 6.7 | 4.3 | 55 | 9.3 | 5.1 | 27.6 | <0.0001 |
| Conduct symptoms[b] | | | | | | | | | | | |
| Anxious subjects[a] | 18 | 0.5 | 0.9 | 11 | 0.6 | 1.3 | 15 | 1.8 | 1.5 | 7.2 | <0.03 |
| Nonanxious subjects[a] | 52 | 0.4 | 0.9 | 59 | 0.4 | 0.9 | 55 | 1.3 | 2.0 | 13.3 | <0.001 |
| Friends[b] | | | | | | | | | | | |
| Anxious subjects | 18 | 1.1 | 1.4 | 11 | 1.4 | 1.3 | 15 | 1.1 | 1.6 | 1.6 | n.s. |
| Nonanxious subjects[c] | 52 | 1.1 | 1.3 | 59 | 0.9 | 1.2 | 55 | 0.3 | 0.8 | 14.6 | <0.001 |
| Family | | | | | | | | | | | |
| Anxious subjects[c] | 18 | 3.2 | 2.9 | 11 | 4.6 | 3.3 | 15 | 6.3 | 4.0 | 6.1 | <0.04 |
| Nonanxious subjects | 52 | 2.9 | 2.4 | 59 | 3.3 | 3.1 | 55 | 3.5 | 2.9 | 1.2 | n.s. |

[a] Mean scores of 8-year-olds and 12-year-olds were significantly different from mean score of 17-year-olds ($p<0.05$, post hoc nonparametric multiple group comparisons, Kruskal-Wallis with chi-square approximations).

[b] Due to the large number of tied values, a median split of the dependent value was performed and then analyzed by chi-square test.

[c] Mean score of 8-year-olds was significantly different from mean scores of 12-year-olds and 17-year-olds; mean score of 12-year-olds was significantly different from mean score of 17-year-olds ($p<0.05$, post hoc multiple group nonparametric comparisons, Kruskal-Wallis with chi-square approximations).

other hand, the rates of problems with family were about the same for all three nonanxious age groups but the anxious 17-year-olds and 12-year-olds had substantially higher rates than the anxious 8-year-olds.

Symptom differences between anxious and nonanxious subjects for each age group are presented in table 4. Every age group of anxious children had significantly more depression and mood difficulties than comparable groups of nonanxious children. The anxious 8-year-olds also reported significantly more attention deficit disorder and acting out symptoms and more physiological complaints than nonanxious 8-year-olds. The anxious 12-year-olds, in the beginning of the transition to adolescence, reported significantly more difficulty with school, self-image, oversensitivity, and concentration than nonanxious 12-year-olds. The anxious 17-year-olds also had significantly higher rates of problems with family than did nonanxious 17-year-olds.

## DISCUSSION

The data from this community study indicate that anxiety concerns similar to those which constitute anxiety disorders in *DSM-III* were the most frequently

**TABLE 4. Anxiety Symptom Scores on the Child Assessment Schedule and the Revised Children's Manifest Anxiety Scale of Anxious and Nonanxious 8-, 12-, and 17-Year-Olds[a]**

| | Score | | | | | |
|---|---|---|---|---|---|---|
| | Anxious Subjects | | Nonanxious Subjects | | | |
| Instrument and Symptom | Mean | SD | Mean | SD | Z | p |
| Child Assessment Schedule | | | | | | |
| Attention deficit disorder symptom complex | | | | | | |
| 8-year-olds | 3.4 | 3.0 | 1.0 | 1.5 | 3.46 | <0.0005 |
| Depression symptom complex | | | | | | |
| 8-year-olds | 7.1 | 5.8 | 3.9 | 2.7 | 1.99 | <0.05 |
| 12-year-olds | 8.6 | 3.6 | 4.2 | 3.6 | 3.63 | <0.0003 |
| 17-year-olds | 9.5 | 4.2 | 5.3 | 3.0 | 3.54 | <0.0004 |
| Mood | | | | | | |
| 8-year-olds | 10.7 | 6.5 | 6.1 | 3.4 | 2.77 | <0.006 |
| 12-year-olds | 9.8 | 2.6 | 6.4 | 3.6 | 3.38 | <0.0007 |
| 17-year-olds | 13.3 | 4.1 | 8.2 | 3.7 | 3.84 | <0.0001 |
| Acting out | | | | | | |
| 8-year-olds | 8.5 | 4.0 | 5.0 | 2.7 | 3.26 | <0.002 |
| Physical complaints | | | | | | |
| 8-year-olds | 4.1 | 3.1 | 2.2 | 2.0 | 2.36 | <0.02 |
| 12-year-olds | 2.6 | 1.7 | 1.4 | 1.5 | 2.24 | <0.03 |
| 17-year-olds | 4.3 | 3.6 | 1.5 | 1.8 | 2.89 | <0.004 |
| School | | | | | | |
| 12-year-olds | 3.2 | 2.6 | 1.4 | 2.0 | 2.50 | <0.02 |
| 17-year-olds | 1.9 | 1.7 | 0.9 | 1.8 | 2.16 | <0.03 |
| Self-image | | | | | | |
| 12-year-olds | 3.3 | 2.5 | 1.5 | 1.0 | 2.60 | <0.01 |
| 17-year-olds | 2.2 | 1.3 | 1.4 | 1.2 | 2.13 | <0.04 |
| Oppositional symptom complex | | | | | | |
| 17-year-olds | 1.6 | 1.3 | 0.9 | 1.2 | 2.13 | <0.04 |
| Family | | | | | | |
| 17-year-olds | 6.3 | 4.0 | 3.5 | 2.9 | 2.72 | <0.007 |
| Revised Children's Manifest Anxiety Scale | | | | | | |
| Physiological subscale | | | | | | |
| 8-year-olds | 5.1 | 2.5 | 3.6 | 1.8 | 2.55 | <0.02 |
| 17-year-olds | 4.5 | 3.0 | 2.4 | 1.8 | 2.63 | <0.009 |
| Oversensitive subscale | | | | | | |
| 12-year-olds | 6.1 | 2.3 | 3.7 | 2.4 | 2.67 | <0.008 |
| 17-year-olds | 5.9 | 3.2 | 3.8 | 2.2 | 2.14 | <0.04 |
| Concentration subscale | | | | | | |
| 12-year-olds | 3.1 | 1.9 | 1.8 | 1.8 | 2.21 | <0.03 |

[a] All analyses used the Wilcoxon test of significance with the normal approximation. Even though standard deviations were not used in these tests, they are reported as a convenience for the reader.

endorsed items on both the Child Assessment Schedule and the Parents' Child Assessment Schedule in 8-, 12-, and 17-year-olds. In a previous study using a different structured interview and somewhat different age groups (14- to 16-year-olds) (12), we found anxiety disorders to be the most prevalent diagnoses. Similarly, Myers et al. (21) reported anxiety disorders to be the most prevalent diagnoses in an adult community sample. These community studies also show consistent sex differences: girls at all ages reported higher rates of anxiety than boys. Recently, Costello et al. (22), using the Diagnostic Interview Schedule for Children, reported that 8.9% of the children in a pediatric primary care setting had some type of anxiety disorder. Bird et al. (23), also using the Diagnostic Interview Schedule for Children, reported that 81 of 777 children 4–16 years old in Puerto Rico had some type of anxiety disorder. Bird et al. also found that nearly half (49.5%) of their general population sample had a *DSM-III* diagnosis. When these researchers also required a Child Global Assessment Scale of less than 61 for a diagnosis, they found that the prevalence of overall disorders dropped from 49.5% to 17.9%. This latter finding underscores the necessity in general population studies of using some instrument to measure the impairment of adaptive functioning in addition to a *DSM-III* diagnosis. This inclusion would have aided the present study.

Although the rates of anxiety symptoms were fairly similar in our three age groups, the type and content of anxiety varied with age. The rates for fear of strangers and fear of separation were lower in the older adolescents, as were somatic complaints; the rates for interpersonal concerns, social fears, and anxiety about personal adequacy were higher in the older adolescents. The comorbidity data suggest that children and adolescents who manifest higher rates of one type of anxiety may also be at risk for other forms of anxiety.

Given the cross-sectional nature of the current study, this hypothesis is speculative and can be confirmed only by longitudinal data.

Across the three age groups, anxious children and adolescents manifested some interesting behavioral differences when compared with nonanxious children and adolescents. Anxious and nonanxious subjects showed similar rates across age groups in the nonanxiety symptoms of depression, acting out, and conduct disorder. However, each age group of anxious subjects had consistently higher levels of symptoms in each category of pathology than did comparable age groups of nonanxious subjects. Therefore, patterns of nonanxiety psychopathology across the age groups were qualitatively similar; anxious and nonanxious subjects differed only in symptom quantity. However, anxiety appears to have a more negative consequence on interpersonal relationships. Nonanxious adolescents had lower rates of problems with peer relations than anxious adolescents. Although anxious and nonanxious 8-year-olds had similar ratings on peer relations, the anxious 17-year-olds had significantly poorer peer relationships than nonanxious 17-year-olds. All three age groups of nonanxious subjects had similar rates of difficulties with family, but the older anxious subjects had substantially higher rates of difficulties than the younger subjects. These data suggest that anxiety exerts its most detrimental effect over time on the interpersonal spheres of functioning.

The anxious 8-year-olds had more symptoms of all types of psychopathology than did nonanxious 8-year-olds. Anxious 12-year-olds had more difficulty in school, poorer self-images, and more symptoms of psychopathology than their nonanxious peers. Finally, anxious 17-year-olds had significantly more behavioral problems, mood problems, somatic complaints, school difficulties, and poor self-concepts than did nonanxious 17-year-olds.

Although the limitations of this cross-sectional study must be considered, the current data suggest that anxiety has a negative influence on a broad range of behaviors and that this negative impact increases and becomes even more detrimental with age, particularly in the inter- and intrapersonal domains. This supports the view expressed by Achenbach (24) that anxiety in children and adolescents should not be viewed as an encapsulated entity independent of the development of other related problems and competencies. Replication of these data by longitudinal studies is an important research priority, and early detection and treatment of anxiety disorders are important clinical priorities for the future.

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# Correlates of Anxiety in Psychiatrically Hospitalized Children and Their Parents

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*The authors separated 100 children hospitalized in a child psychiatry service into three groups according to their level of anxiety on the basis of the responses of the children and their parents to diagnostic interviews. Differentiation of the groups of children was validated by independent test instruments. Results of tests administered to the children and their parents revealed significant relationships between anxiety in the adults and in the children. In addition, parents of anxious children reported more SCL-90-R symptoms as well as more negative family relations than parents of nonanxious children and the more severely anxious children had higher rates of dysthymia and negative life events.*
(Am J Psychiatry 1990; 147:319–323)

Anxiety disorders are the single largest mental health problem in the United States, more prevalent than depression and substance abuse in both adults (1, 2) and adolescents (3). The ubiquitous nature of anxiety, however, challenges the very definition of this disorder. *DSM-III-R,* appendix C, defines anxiety as apprehension, tension, or uneasiness that stems from the anticipation of internal or external danger. Manifestations of anxiety and fear are equated in this definition; they include motor tension, autonomic hyperactivity, apprehensive expectation, and vigilance and scanning.

Current psychiatric nomenclature specifies several anxiety disorders with a childhood onset (4). These include separation anxiety disorder, avoidant disorder of childhood or adolescence, and overanxious disorder. Simple phobia may also be included in the childhood disorders despite the fact that it is listed among the adult anxiety disorders. Therefore, several types of anxiety can be differentiated among children. Although each has distinguishing features and may occur alone, the various anxiety disorders can overlap (5).

A few reports have investigated clinically referred anxious children. Last et al. (6) examined the *DSM-III* diagnostic categories of separation anxiety and overanxious disorder in a clinical group of 69 children and adolescents. Last et al. (7) also studied phobic disorders and separation anxiety disorder in another study that included inpatient children. This investigation supported the use of *DSM-III* criteria for differentially diagnosing the two anxiety disorders. Mattison and Bagnato (8) researched the validity of overanxious disorder in boys 8 to 12 years old who were inpatients; they used various scales and demonstrated both convergent and discriminant validity. Finally, Alessi and Magen (9) documented the occurrence of panic disorder as well as its relationship to separation anxiety and depression in a child psychiatry inpatient setting.

Increasing evidence from varying approaches suggests that adult anxiety states are often likely to be preexisting in childhood (9). Since these disorders may be later manifested in adulthood, childhood anxiety disorders deserve and require active investigation (10). Although the adult diagnoses of agoraphobia and agoraphobia with panic attacks have not been reported in children, there is evidence that separation anxiety is at the root of agoraphobia (11). In a review of the histories of severely impaired agoraphobic inpatients, Klein (12) found that half had had separation anxiety and difficulty in adjusting to school during childhood. Likewise, Gittelman-Klein and Klein (13) suggested that children with school phobia and adults with anxiety may share a common psychopathological process because adults and children with phobia had similar positive responses to imipramine.

The possible progression of anxiety from childhood to adulthood warrants the study of this area from various aspects, including the frequency and correlates of this disorder. Assessment, diagnosis, and treatment of anxiety disorder are major tasks for clinicians and researchers if this prevalent psychiatric disorder is to be ameliorated or prevented.

This study was undertaken to investigate specific aspects of childhood anxiety that previous studies on childhood anxiety have overlooked. Specifically, we systematically identified and quantified the severity of anxiety in a group of psychiatrically hospitalized children. We validated the division of our anxiety subjects

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through the use of independent instruments that assess anxiety symptoms. We also investigated the coexistence of psychiatric disorders in the more severely anxious children. Because the role of family dysfunction as it relates to anxiety disorders is in need of urgent attention, we used the SCL-90-R to study the characteristics of the parents of children with and without anxiety. We also applied the Personality Inventory for Children and the Life Events Checklist in the hope that results from instruments such as these will further elucidate the nature of anxiety in hospitalized children.

## METHOD

### *Subjects and Procedure*

The study group consisted of 100 children admitted to an inpatient child psychiatry service in a community mental health center affiliated with the University of Missouri-Columbia. To obtain our group of 100 children, 155 children consecutively admitted to the inpatient service were evaluated. Of these 155 children, 42 were excluded either because of age (outside the 7–12-year-old age group) or because of a full-scale WISC-R score of less than 70, which may call into question the reliability of the interview results. After 100 children had qualified for the study, the gathering of subjects was stopped.

All children and their parents consented to participation in the study after its nature had been explained to them.

During the first week of admission to the inpatient unit, the children were interviewed by a doctoral candidate in clinical psychology trained to administer the Diagnostic Interview for Children and Adolescents (14) and the Diagnostic Interview for Children and Adolescents—Parents Version (14). The same interviewer also administered the Revised Children's Manifest Anxiety Scale (15), the Life Events Checklist (16), and the Piers-Harris Children's Self-Concept Scale (17). In addition, all parents (usually the patient's mother) were interviewed and completed self-report questionnaires.

The children were 7–12 years old; 73 were boys, and 27 were girls; 91 were Caucasian, and nine were black. According to Hollingshead and Redlich's rating of socioeconomic status (18), one child was in class I, five were in class II, 50 were in class III, 34 were in class IV, and 10 were in class V.

Information from both the children and their parents was used to assess the severity of anxiety for each child. The children diagnosed as having an anxiety disorder (overanxious, separation anxiety, or phobia) according to their parents' reports (the Diagnostic Interview for Children and Adolescents—Parents Version) and their own reports (the Diagnostic Interview for Children and Adolescents) were considered severely anxious. Children diagnosed as having an anxiety disorder according to either their parents' or their own reports were considered possibly anxious. Children without a diagnosis of anxiety disorder according to their parents' and their own reports were considered nonanxious.

Results of the diagnostic interviews for children and parents could not be combined due to the distinctiveness of the two diagnostic interviews. Attempts have been made to resolve this disagreement problem by 1) letting the clinician make the final decision as to the child's diagnosis, 2) reporting only the child's response or reporting only the parent's response, or 3) reporting only diagnoses that are generated by both the diagnostic interview for children and the diagnostic interview for parents (concordant diagnoses). This last alternative is the most stringent because it requires full agreement between the parent and child and is the one we chose to define anxiety in the children.

### *Instruments and Statistical Analyses*

Both children's and parents' instruments were used in the present study. Children's questionnaires consisted of the Diagnostic Interview for Children and Adolescents (14), the Revised Children's Manifest Anxiety Scale (15), the Piers-Harris Children's Self-Concept Scale (17), and the Life Events Checklist (16). Instruments administered to the parents consisted of the Diagnostic Interview for Children and Adolescents—Parents Version (14), the SCL-90-R (19), and the Personality Inventory for Children (20). The SCL-90-R assessed symptoms in the parents rather than in the children.

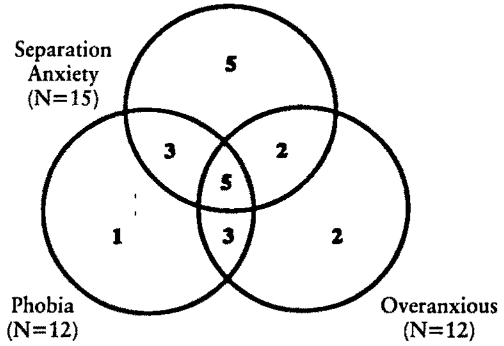
Interval data were analyzed by using the Mann-Whitney U test. We hypothesized that some items on some instruments would be related to greater severity of anxiety disorders—that more severely anxious patients would have higher scores on some items. If the data were dichotomous the Bartholomew test (21, 22) was used, and if the data were continuous the Jonckheere-Terpstra (23, 24) was used. The Bartholomew test is of proportions when samples are qualitatively ordered (i.e., anxious, possibly anxious, and nonanxious). It is not distributed like the chi-square but typically refers to special tables through the measure c, which is a function of sample size. The Jonckheere-Terpstra was used to test against the alternative that group means are ordered. We report the uncorrected alpha values obtained for all analyses. All tests were two-tailed.

## RESULTS

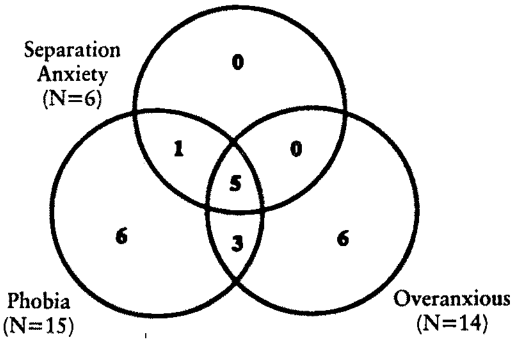
No differences in race (Caucasian versus black) (Bartholomew's $\chi^2=1.4$, $c=0.35$, $p>0.10$) or sex (Bartholomew's $\chi^2=2.7$, $c=0.35$, $p>0.05$) were found among the three groups of children, nor were there significant differences among the groups in socioeconomic status

**FIGURE 1. Overlap of Anxiety Disorder Diagnoses in 21 Psychiatrically Hospitalized Children With Severe Anxiety**[a]

Diagnostic Interview for Children and Adolescents



Diagnostic Interview for Children and Adolescents-Parent Version



[a]The numbers in each area represent the numbers of children.

(Z=0.23, p>0.82) or age (Z=−1.2, p>0.22) by the Jonckheere-Terpstra.

Twenty-one of the 100 children had severe anxiety: both the children and their parents reported a sufficient number of anxiety symptoms on their respective diagnostic interviews for the children to meet criteria for at least one anxiety diagnosis (phobia, overanxious disorder, or separation anxiety). Forty-eight children had possible anxiety: they were diagnosed as having an anxiety disorder according to either their parents' or their own diagnostic interviews. The remaining 31 children had no anxiety diagnosis according to their own or their parents' diagnostic interviews. Figure 1 shows the overlap of diagnoses of specific anxiety disorders in the severely anxious children according to their own interviews and their parents' interviews. None of the children was given a diagnosis of obsessive-compulsive disorder.

Table 1 shows the results of the Jonckheere-Terpstra tests on the Revised Children's Manifest Anxiety Scale, the Piers-Harris Children's Self-Concept Scale, the Life Events Checklist, the Personality Inventory for Children, and the SCL-90-R. In all of the analyses shown in table 1, it is clear that the more severely anxious children and parents had higher rates of negative symptoms as revealed through the various instruments.

The mean number of coexisting Diagnostic Interview for Children and Adolescents diagnoses was calculated for each of the three groups of children. Possible diagnoses consisted of attention deficit disorder, major depressive disorder, oppositional disorder, conduct disorder, mania, and elimination problems. The 21 children with serious anxiety had a mean of 2.2 diagnoses. The 48 children with possible anxiety had a mean of 1.6 diagnoses, and the 31 nonanxious children also had a mean of 1.6 diagnoses. Comorbidity among these three groups was not significant ($\chi^2=2.2$, $p>0.12$, Mann-Whitney U test).

Finally, the more severely anxious children had significantly higher rates of dysthymic disorder (Bartholomew's $\chi^2=6.1$, $c=0.35$, $p<0.05$).

## DISCUSSION

The major findings of this study are as follows. First, children and their parents in combination identified the most severe cases of childhood anxiety as validated by independent test instruments. Second, significant relationships were found between parents' anxiety and children's anxiety. Third, parents of children with anxiety disorders reported more SCL-90-R symptoms associated with problems such as somatization, phobic anxiety, depression, and hostility than parents of nonanxious children. Fourth, as admitted by parents of children with anxiety disorders, there were troubled relations within the family. Finally, the prevalence of the diagnosis of dysthymic disorder and negative life events was greater in the more severely anxious patients.

Before further discussing the findings, we must point out that the results from this inpatient study cannot be generalized to the general or outpatient population and thus must be viewed with caution. The findings of this study are also not applicable to children with low intellectual abilities because such children were eliminated from our study group. Finally, the results obtained do not prove direct causal relationships and are subject to clinical interpretation.

Despite these limitations, the present study provides data on the most serious types of anxiety disorders in children. This study required full agreement between parents and children in the categorization of severe anxiety in the children. Applying this criterion, we found that approximately one out of five children in an inpatient group of 100 was severely anxious.

The validation of results obtained from the child and a parent was shown through a variety of well-standardized anxiety scales. There was a significant difference between anxious and nonanxious children in Revised Children's Manifest Anxiety Scale total scores (including physiological, worry, and concentration subscales). This implies that the severity of anxiety in the children classified as severely anxious was reflected in high scores of the Revised Children's Manifest Anxiety Scale. The severely anxious children also had more symptoms on the Piers-Harris Children's Self-Concept Scale. Finally, the Personality Inventory for Children

**TABLE 1. Scores of 100 Severely, Possibly, or Not Anxious Children and Their Parents on Ratings of Anxiety**

| | Children With No Anxiety (N=31) | | Children With Possible Anxiety (N=48) | | Children With Severe Anxiety (N=21) | | | |
|---|---|---|---|---|---|---|---|---|
| Instrument | Mean | SD | Mean | SD | Mean | SD | Z[a] | p |
| Administered to child; children's scores reported | | | | | | | | |
| Revised Children's Manifest Anxiety Scale | 9.6 | 7.5 | 12.8 | 8.0 | 13.8 | 6.9 | 2.1 | 0.03 |
| Piers-Harris Children's Self-Concept Scale[b] | 8.6 | 3.2 | 7.3 | 3.5 | 6.8 | 3.6 | −2.0 | 0.04 |
| Life Events Checklist | 4.1 | 2.8 | 5.3 | 3.6 | 6.2 | 3.0 | 2.4 | 0.01 |
| Administered to parent | | | | | | | | |
| Children's scores reported | | | | | | | | |
| Personality Inventory for Children | | | | | | | | |
| Depression | 17.5 | 7.1 | 20.2 | 9.2 | 22.1 | 8.7 | 2.3 | 0.02 |
| Anxiety | 10.5 | 4.2 | 13.3 | 6.0 | 15.0 | 5.0 | 3.3 | 0.001 |
| Family relation | 9.3 | 5.5 | 12.2 | 6.2 | 15.3 | 7.9 | 3.1 | 0.001 |
| Parents' scores reported | | | | | | | | |
| SCL-90-R[c] | | | | | | | | |
| Somatization | 0.5 | 0.5 | 0.7 | 0.7 | 1.0 | 0.7 | 2.5 | 0.01 |
| Obsessive-compulsive | 0.6 | 0.5 | 0.8 | 0.7 | 1.1 | 0.9 | 2.2 | 0.02 |
| Interpersonal sensitivity | 0.6 | 0.5 | 0.8 | 0.7 | 1.1 | 1.0 | 2.0 | 0.04 |
| Depression | 0.7 | 0.7 | 1.0 | 0.8 | 1.3 | 0.9 | 2.6 | 0.01 |
| Anxiety | 0.5 | 0.5 | 0.7 | 0.6 | 1.0 | 0.9 | 2.8 | 0.005 |
| Hostility | 0.4 | 0.4 | 0.7 | 0.8 | 0.8 | 0.8 | 2.3 | 0.02 |
| Phobic anxiety | 0.2 | 0.3 | 0.2 | 0.4 | 0.6 | 0.9 | 2.5 | 0.01 |

[a] All analyses for differences among the ordered severity groups were done by using the Jonckheere-Terpstra nonparametric test. The large sample approximation yields Z scores.
[b] Low scores indicate more anxiety symptoms.
[c] Bonferroni p level is 0.005.

anxiety scale provided further validation for a clear division between anxious and nonanxious children; the children with severe anxiety also displayed the most anxious personality characteristics.

Although no causal relationship between parental dysfunction and childhood psychopathology could be determined, the SCL-90-R data as well as the Personality Inventory for Children family relations scale analysis certainly suggest a link between dysfunctional family behavior and anxiety in the child. Such a link underscores the importance of family dynamics as an influence on the child's ability to adjust.

The Personality Inventory for Children findings emphasize the parental discord and disharmony in the families of severely anxious children. Although such disruptive family influences may contribute to the development of anxiety in the child, coexisting factors such as genetic and/or biological influences may also contribute. These are beyond the scope of this study.

The new finding that the parents of children with severe anxiety had significantly higher hostility scores than the parents of the other children broadens our understanding of the nature of childhood anxiety. Hostile or critical parental attitudes may well lead to a child's perception and anticipation of danger (an essential part of the definition of anxiety).

The finding that the severely anxious children had higher depression scores than the other children may be evidence in support of Seligman's two-phase theory (25), which posits that anxiety develops first and depression is later superimposed on the anxiety symptoms. Since the more severely anxious children had a higher rate of negative life events than the other children in our study, we can infer that the severely anxious group was exposed to more threats and stress than the other two groups. Thus, according to Seligman's theory, it follows that the severely anxious children who were exposed to more stressful events would also have more depression than the rest of the children.

In conclusion, the use of both children and their parents to categorize children according to the severity of their anxiety enabled us to further understand the nature of anxiety in children. The fact that differences emerged between children who were categorized as possibly anxious and children who were severely anxious underscores the importance of using information from both the child and the parent in the clinical setting. Finally, issues such as the problem of causation might be resolved through longitudinal studies.

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# Evaluation of a Mental Illness Awareness Week Program in Public Schools

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*The authors evaluated the impact of a Mental Illness Awareness Week program on the attitudes of adolescents attending public school toward seeking help for mental health problems and toward psychiatrists. Most students involved in the program liked it and indicated that they were interested in learning more about mental health topics. Students in the program showed more favorable attitudes toward seeking help and toward psychiatrists than a comparison group of students who did not participate in the program. The authors discuss the evidence for enduring effects of the program. The results support continued development of Mental Illness Awareness Week programs for adolescents in the public schools.*

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In 1983 APA's Division of Government Relations worked with the U.S. Congress to establish an annual Mental Illness Awareness Week. In addition to promoting public awareness of mental health issues, Mental Illness Awareness Week was intended "to promote the best interests of patients and those actually or potentially making use of mental health services" (1). Although programs presented as part of Mental Illness Awareness Week have gained strong national recognition since 1983, there is a lack of research on the impact of these educational programs and preventive efforts. However, preventive mental health programs specifically for adolescents were researched well before the institution of Mental Illness Awareness Week (2–4). More recent examples that do not fall under the Mental Illness Awareness Week rubric have focused on the impact of programs for adolescents in drug education (5, 6), suicide prevention (7–9), and sex education (10). One finding in this area of research has been that improvement in factual knowledge may not correlate well with changes in attitudes and behavior (11–13).

Promoting positive attitudes toward mental health is important for support of mental health goals and is an integral part of any preventive educational approach (14). This is especially true for adolescents: psychiatric and behavioral problems have replaced infectious disease as the major cause of morbidity and mortality among adolescents in the United States over the past 30 years. Increasingly, adolescent life styles and risk-taking behavior are influencing the so-called new morbidities of youth—depression, substance abuse, physical and sexual abuse, and teenage pregnancy (15).

With these needs in mind we developed a Mental Illness Awareness Week program for adolescents in public middle schools and high schools. We measured the students' previous exposure to talks about various mental health topics in school. Our goals included measuring students' attitudes toward the program itself, their attitudes toward psychiatrists and toward seeking help for psychiatric problems, and their desire to hear more about mental health issues.

## METHOD

In 1986, middle schools and senior high schools in our area were notified through an announcement flyer that psychiatric physicians would be available during Mental Illness Awareness Week to speak to students about topics such as psychiatry, drugs and alcohol, suicide, and depression. Two middle schools and eight high schools requested such presentations. In preparation for these presentations, 20 residents from the psychiatry programs of Baylor College of Medicine and the University of Texas, Houston, attended three training sessions. In the first session, procedures for contacting the schools and teachers were reviewed and legal and public affairs issues were discussed. In the second session, several residents presented information about teenage suicide and depression as well as on alcohol and drug abuse. The third session was a seminar on the topic "How to give a talk in the schools" that addressed practical issues such as working in a noisy classroom and dealing with disruptive students. Residents were given an outline of topics they should cover and were instructed to tell the students that school counselors were available as a first step for help. Manuals on available youth services were also given to residents for distribution to the school counselors.

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Teachers were asked if they would like to volunteer their classes for a time that coincided with the visit of the residents. Students were assembled for the 45-minute presentations in single classrooms, combined classrooms, or large assembly halls. Students who heard the presentations comprised the experimental group and were asked to fill out questionnaires at the end of the presentations. Teachers were given additional questionnaires and asked to distribute these that same day to students in similar grades who had not heard the presentations. These students comprised the comparison group. Enough comparison group questionnaires were handed out to achieve a ratio of at least 10 to 1 (experimental to comparison) to allow for adequate statistical testing. The questionnaires were collected by the teachers and mailed back to the authors in self-addressed envelopes. It should be noted that assignment to the two groups was not done randomly. However, since assignment was made on the basis of teachers' preferences or schedule compatibility and not on student self-selection, we think that selection biases in the data would not be strong unless teacher and student preferences were intercorrelated.

The experimental group was asked to indicate what they thought of the talk on a 5-point scale on which 1=liked very much and 5=disliked very much. They also were asked whether the talk was helpful in any way by responding yes, no, or don't know and then to explain their answer. The remainder of the questions were the same for both groups. All of the students were asked about their previous exposure to various mental health talks in schools as well as their interest in hearing more about relevant topics. They were asked to indicate their attitudes toward psychiatrists by circling responses on a 5-point scale on which 1=very positive and 5=very negative. Students also indicated the likelihood that they would seek a psychiatrist's help for problems on a 5-point scale on which 1=definitely would and 5=definitely would not.

The experimental group included 1,380 students; 477 were boys, 831 were girls, and 72 did not specify their sex. Two hundred twenty-six (16.4%) of these students were in grade 12, 176 (12.8%) were in grade 11, 235 (17.0%) were in grade 10, 374 (27.1%) were in grade 9, 82 (5.9%) were in grade 8, 86 (6.2%) were in grade 7, and 201 (14.6%) were in grade 6. The mean grade was 9.3.

The comparison group included 282 students; 93 were boys, 176 were girls, and 13 did not specify their sex. Sixty-one (21.6%) were in grade 12, 61 (21.6%) were in grade 11, 63 (22.3%) were in grade 10, 52 (18.4%) were in grade 9, four (1.4%) were in grade 8, nine (3.2%) were in grade 7, and 32 (11.3%) were in grade 6. The mean grade was 9.9.

The difference in mean grade between the comparison and experimental groups was significant (t=4.74, df=1660, p=<0.001). There is no obvious explanation for this difference: teachers were asked to distribute the questionnaires to comparable grades. No significant difference was found between the comparison and experimental groups in sex.

## RESULTS

In response to the question, "What did you think of the talk?" 782 (56.7%) of the students in the experimental group responded, "Liked very much"; 356 (25.8%), "Liked some"; 182 (13.2%), "Neutral"; 17 (1.2%), "Disliked some"; and 15 (1.1%), "Disliked very much"; 28 (2.0%) of the students did not respond to this question. When asked, "Was this a talk that was helpful to you in any way?" 956 (69.3%) of the students in the experimental group answered, "Yes," 171 (12.4%) answered, "No," and 223 (16.2%) answered, "Don't know"; 30 (2.2%) of the students did not answer this question.

The responses of the students when asked to explain their answers to the question regarding whether the presentations were helpful were sorted into 18 categories. This allowed for assessment of both the benefits and criticisms of the presentations. Multiple responses were allowed for each student, and 427 (30.9%) of the students did not give any answers. Two hundred forty-two (21.5%) of the responses indicated that students obtained information on drugs and alcohol (e.g., "Helped me know more about such drugs as crack, designer drugs." "I had no idea angel dust (PCP) could make you so paranoid."), 189 (16.8%) of the responses indicated that the students gained nonspecific information ("I found out about things I didn't know."), and 115 (10.2%) were positive in other ways ("It was encouraging."). Responses also indicated that the students gained information about psychiatry (N=63; 5.6%), depression and suicide (N=50; 4.4%), other mental disorders (N=21; 1.9%), and other medical knowledge (N=11; 1.0%).

Fifty-one (4.5%) of the responses indicated that students gained help for problems related to themselves ("This talk gave me second thoughts about . . . like getting back at my parents or killing myself because of boys."), and 31 (2.8%) of the responses indicated that personal insight was gained ("Helped me understand myself in many ways."). However, 72 (6.4%) of the responses indicated a denial of problems ("I have none of those problems they talked about."). Fifty-seven (5.1%) of the responses indicated that help was obtained for problems related to others ("I know someone who drinks."), and 44 (3.9%) indicated that the students learned about others ("Tells you a little about someone else's life."). Forty-one (3.6%) of the responses indicated that the talk would help prevent future problems ("Encouraged me not to use drugs in future.").

Some assessments were negative: 76 (6.8%) of the responses noted redundancy in the presentations ("I have heard it before."); seven (0.6%) noted nonspecificity ("Could have gone into more detail."); and six (0.5%) noted nonunderstandability.

To evaluate the novelty of these presentations, three questionnaire items asked about previous exposure to talks about mental health issues in the schools. To the question, "Has a teacher or other professional ever talked about psychiatrists before in this school?" 477 (34.6%) of the students in the experimental group and 102 (36.2%) in the comparison group said yes. Forty-three (3.1%) of the students in the experimental group and two (0.7%) of those in the control group did not respond to this question. To the question, "What about depression or suicide?" 684 (49.6%) of the students in the experimental group and 155 (55.0%) in the comparison group said yes. Thirty-eight (2.8%) of the students in the experimental group and two (0.7%) of those in the control group did not answer this question. Finally, to the question, "What about drugs and alcohol?" 1,028 (74.5%) of the students in the experimental group and 222 (78.7%) in the comparison group said yes. The differences between the experimental and comparison groups were not statistically significant.

The effect of the presentations on students' feelings toward psychiatrists was measured. Using an analysis of variance, responses of the experimental and comparison groups to the question, "What are your feelings about psychiatrists?" were compared according to the students' previous exposure to talks about psychiatrists and their grade. Main effects were found for groups (experimental versus comparison) ($F=79.0$, $df=1, 1588$, $p<0.001$) and for previous exposure ($F=5.7$, $df=1, 1588$, $p<0.05$). Students' attitudes were generally positive, but those of the experimental group were more positive than those of the comparison group and those of students who had had previous exposure to talks about psychiatrists were more positive than those of students who had not. There were no significant interaction effects, and grade was not a significant covariate.

The effect of the presentations on students' attitudes toward seeking a psychiatrist's help was measured by the question, "If you had a problem (like depression, suicidal feelings, stress, nervousness, or problems with alcohol or drug use), how likely is it that you would seek a psychiatrist's help?" Analyses of variance were applied to the experimental versus comparison groups, previous exposure to talks on the three areas of mental health issues in the school (psychiatrists, depression and suicide, drugs and alcohol), and grade. In each analysis, a main effect was found for group: students in the experimental group who had been exposed to previous talks were more likely than students in the comparison group exposed to previous talks to seek psychiatric help ($F=6.5$, $df=1, 1559$, $p<0.05$ for talks about psychiatrists; $F=6.2$, $df=1, 1569$, $p<0.05$ for talks about depression and suicide; and $F=6.0$, $df=1, 1571$, $p<0.05$ for talks about drugs and alcohol). There were also main effects for previous exposure to talks on mental health issues: previous exposure to talks on any of the three issues resulted in a greater likelihood of seeking psychiatric help (for talks on psychiatrists, $F=4.98$, $df=1, 1559$, $p<0.05$; for talks on depression and suicide, $F=7.9$, $df=1, 1569$, $p<0.01$; for talks on drugs and alcohol, $F=15.7$, $df=1, 1571$, $p<0.001$).

There were no interaction effects in the analyses that were applied to the experimental versus control groups, previous exposure to talks on the three areas of mental health issues in the school, and grade. In each analysis, however, grade was a significant covariate (for talks on psychiatrists, $F=5.39$, $df=1, 1559$, $p<0.05$; for talks on depression and suicide, $F=5.68$, $df=1, 1569$, $p<0.05$; for talks on drugs and alcohol, $F=7.03$, $df=1, 1571$, $p<0.01$). A Pearson's correlation of grade with likelihood of seeking psychiatric help was 0.07 ($p<0.01$, $df=1594$), indicating a small but significant trend for students in higher grades to be less likely to seek help.

To evaluate students' help-seeking behavior, they were asked, "What would be the first step in getting help for one of the problems mentioned above?" Responses were sorted into 15 categories, and multiple responses by each student were allowed. The number of students in each group giving responses for each category is shown in table 1. Frequent categories for the experimental group included "Unspecified—help implied," tell family, tell friend, tell counselor, and tell psychiatrist. Infrequent categories included "Don't know," self-treatment, and "Would not get help." The impact of the presentations on first-step choices was measured by comparing categories of responses made by students in the experimental and comparison groups. The experimental group provided responses fitting categories of telling a psychiatrist, counselor, or teacher significantly more frequently than the comparison group. The comparison group provided responses significantly more frequently in the categories of telling family and admitting having a problem than the experimental group.

The effectiveness of the talk on students' interest in hearing more about mental health issues was measured by comparing the responses of students in the experimental and comparison groups to the question, "Would you like to hear more about topics like those talked about today [or, for the comparison group, about topics like those listed above]?" The experimental group indicated a significantly greater desire to hear more: 936 (67.8%) of these students said yes, compared with 164 (58.2%) of the comparison group ($\chi^2=29.5$, $df=1$, $p<0.001$). One hundred seventy-one (12.4%) of the students in the experimental group and 14 (5.0%) of those in the comparison group did answer this question. However, examining these results by each grade resulted in expected frequencies that were too low within each cell for meaningful statistical testing.

Students who said yes were asked to list the topics they would like to hear more about. Responses were sorted into 16 categories, and multiple responses were allowed for each student. The numbers of students providing responses for each category are shown in

**TABLE 1. First Step in Getting Help Listed by Students Who Did or Did Not Attend Mental Illness Awareness Week Programs in Their Schools**

| First Step Listed | Students Who Attended Programs (N=1,380)[a] N | % | Students Who Did Not Attend Programs (N=282) N | % | $\chi^2$ (df=1) | Significance |
|---|---|---|---|---|---|---|
| Tell family | 222 | 16.2 | 61 | 21.6 | 5.0 | $p<0.05$ |
| Tell friend | 171 | 12.4 | 35 | 12.4 | 0.0 | n.s. |
| Tell psychiatrist | 132 | 9.6 | 16 | 5.7 | 3.9 | $p<0.05$ |
| Tell medical authority (unspecified) | 62 | 4.5 | 15 | 5.3 | 0.2 | n.s. |
| Tell religious authority | 6 | 0.4 | 5 | 1.8 | 4.5 | —[b] |
| Tell counselor | 135 | 9.8 | 10 | 3.5 | 10.7 | $p<0.005$ |
| Tell teacher | 38 | 2.8 | 1 | 0.4 | 4.9 | $p<0.05$ |
| Self-treatment | 32 | 2.3 | 7 | 2.5 | 0.0 | n.s. |
| Unspecified—help implied (e.g., telling someone who cares) | 313 | 22.7 | 75 | 26.6 | 1.9 | n.s. |
| Other specified help (e.g., call 911) | 29 | 2.1 | 5 | 1.8 | 0.0 | n.s. |
| Don't know | 50 | 3.6 | 11 | 3.9 | 0.0 | n.s. |
| Would not get help | 10 | 0.7 | 2 | 0.7 | 0.0 | —[b] |
| Denial of problem | 6 | 0.4 | 3 | 1.1 | 1.2 | —[b] |
| Admit having a problem | 47 | 3.4 | 32 | 11.3 | 30.9 | $p<0.001$ |
| Other | 33 | 2.4 | 4 | 1.4 | 0.6 | n.s. |

[a] Not all students responded to the question.

[b] Expected frequencies were too low to draw conclusions.

table 2. Frequently selected responses for the experimental group included drugs, suicide, alcohol, depression, stress, and "other topics." The responses of the experimental and comparison groups were compared to clarify whether the presentations made a difference to students' interests. For the categories of sexual abuse, child abuse, medical information, emotions, and abortion the expected frequencies were too low to compute valid chi-squares. The percentages of students indicating a desire to hear more about stress, family problems, sex education, and "other topics" in the experimental group were significantly greater than those in the comparison group. However, the percentages of students in the comparison group who said they wanted to know more about alcohol, suicide, and depression were significantly greater than those in the experimental group.

## DISCUSSION

Most of the students who attended the presentations liked them and found them helpful. Students indicated that the talks helped them to learn new things. Drugs and alcohol were most frequently cited as areas that were learned about. This is encouraging given the extent of substance use problems found in schools (15). Other areas reportedly learned about included psychiatry, suicide, and depression. There were no responses indicating a stimulation of ideas that might lead toward drug use or suicidal behavior.

Some responses indicated that the presentations were helpful in a personal way. For example, some students indicated that they learned about themselves or about their own problems, or that the presentations helped to prevent future problems. Although these findings are encouraging, longitudinal studies of changes in attitude or behavior will be important to evaluate possible enduring effects of the presentations. Some students indicated that the presentations were not helpful. It would be useful to understand more about the students who made these responses. An evaluation of a youth suicide prevention program found that subjects who had made previous suicide attempts were more likely than those who had not to give a negative assessment of the program (unpublished 1988 manuscript of D. Shaffer et al.). However, there probably were students who sincerely felt they were relatively free of substantial problems or who found the information presented redundant.

Although attitudes toward psychiatrists on the whole were positive, significantly more of the students who attended the presentations than of those who did not reported liking psychiatrists. This suggests that this type of intervention has a positive impact on attitudes toward psychiatrists. Several factors may contribute to this finding. For example, students may have been impressed by meeting professionals who showed their concern by taking time to talk to them in the schools without financial remuneration. The presence of young professionals who serve as role models may be sufficient in itself to induce attitude change. This difference in attitude may also relate to positive information given during the presentation about psychiatrists. Although these are possibilities, future research should allow for delineation of the effective components for

**TABLE 2. Topics Students Wanted to Hear More About After Attending or Not Attending Mental Illness Awareness Week Programs in Their Schools[a]**

| Topic | Students Who Attended Programs (N=1,380) | | Students Who Did Not Attend Programs (N=282) | | $\chi^2$ (df=1) | Significance |
|---|---|---|---|---|---|---|
| | N | % | N | % | | |
| Drugs | 432 | 31.3 | 93 | 33.0 | 0.3 | n.s. |
| Alcohol | 207 | 15.0 | 65 | 23.0 | 10.5 | $p<0.005$ |
| Suicide | 269 | 19.5 | 82 | 29.1 | 12.3 | $p<0.001$ |
| Depression | 200 | 14.5 | 62 | 22.0 | 9.6 | $p<0.005$ |
| Psychiatry | 29 | 2.1 | 10 | 3.5 | 1.5 | n.s. |
| Teenage pregnancy | 65 | 4.7 | 11 | 3.9 | 0.2 | n.s. |
| Stress | 152 | 11.0 | 7 | 2.5 | 18.7 | $p<0.001$ |
| Sexual abuse (including rape) | 19 | 1.4 | 2 | 0.7 | 0.4 | —[b] |
| Child abuse | 23 | 1.7 | 4 | 1.4 | 0.0 | —[b] |
| Family problems | 46 | 3.3 | 2 | 0.7 | 4.7 | $p<0.05$ |
| Sex education | 43 | 3.1 | 2 | 0.7 | 4.3 | $p<0.05$ |
| Medical information | 19 | 1.4 | 2 | 0.7 | 0.4 | —[b] |
| Emotions | 12 | 0.9 | 1 | 0.4 | 0.4 | —[b] |
| Unspecified problems | 29 | 2.1 | 1 | 0.4 | 3.1 | n.s. |
| Abortion | 4 | 0.3 | 1 | 0.4 | 0.0 | —[b] |
| Other topics | 144 | 10.4 | 1 | 0.4 | 28.6 | $p<0.001$ |

[a] Students could list more than one topic.
[b] Expected frequencies were too low to draw conclusions.

attitude change. An alternative interpretation of this finding might be that the students in the comparison group reflected the possible negative bias of the teachers who chose not to expose them to the presentations. The extent of this bias was not measured in this study.

There was a small but significant trend for the students in higher grades in both the experimental and comparison groups not to seek help. This may relate to a greater reliance on self or on peer groups with maturation or it may relate to the finding that as students age their perception of the risk associated with certain behaviors such as drinking may decrease (16, 17). Also, significantly more of the students who heard the presentation reported that they would be likely to seek a psychiatrist's help. More positive feelings toward psychiatrists as well as a greater likelihood of seeking their help may allow for earlier detection and management of student problems. The residents who gave the presentations were specifically instructed to recommend talking to the school counselor as a first step for getting help. Students who heard the presentation listed telling a counselor significantly more frequently as a first step than did the comparison group, indicating that this message may have been successfully conveyed to some students. Telling family, friends, or teachers are also appropriate first steps for seeking help, but contacting a psychiatrist may not be. The finding that telling a psychiatrist was listed more frequently by those who heard the presentation perhaps reflects greater familiarity with what a psychiatrist is or more positive feelings toward psychiatrists in general. Alternatively, the comparison group listed admitting having a problem more frequently as a first step, which represents a more abstract and possibly less practical response than other good responses.

Certainly, factors beyond those measured here may also contribute to the likelihood that students would seek psychiatric help (18). It will be important, therefore, to determine if the presentations made a difference in students' help-seeking behavior. It will also be important to determine the extent to which attitude change lasts beyond the time of the presentations. The fact that information was collected immediately after the presentations limits the significance of these results. However, having heard previous talks by teachers or other mental health professionals about psychiatrists significantly enhanced attitudes toward psychiatrists and toward seeking help. Similarly, having heard talks about drugs and alcohol or suicide and depression was positively related to attitudes toward seeking help. These findings underline the potential for a durable benefit in attitude change as a result of the intervention. Further research considerations include identifying groups of students who might warrant special targeting for presentations like these.

Both groups of students wanted to hear more about mental health issues, and both listed a wide variety of topics they would like to hear more about. Drugs, suicide, alcohol, and depression were topics listed most frequently by both groups, which might indicate that students have special interest in these areas or attribute importance to them. In addition, there was evidence that the presentations had an impact on students' interest in hearing more, suggested by the finding that significantly more of the experimental group indicated a desire to hear more about these issues. Stress, family problems, sex education, and "other topics" were also listed more frequently by the experimental group as ones they would like to hear more about. This may reflect interest stimulated by the presentations or relate to the possibility of the experimental group's having heard about a wider range of topics.

Although most of the students in both groups reported that they wanted to hear more about these topics, many reported not having heard about them from teachers or other mental health professionals in the schools. Most students indicated that they had not heard talks about psychiatrists before. Nearly half of the students indicated that they had not heard talks about depression or suicide, and about one-fifth said that they had not heard talks about drugs and alcohol. Given the prevalence of these problems in school populations these figures may indicate a need for mental health professionals to increase their involvement in researching and developing mental health interventions in the schools. Any such involvement would likely be novel for many students.

These results illustrate some of the ways in which Mental Illness Awareness Week presentations affected middle and high school students. Potential research directions for the future have been indicated. In considering the costs and benefits of such programs, wider considerations should also include the impact on psychiatrists in training and on those who volunteer to talk in schools, as well as on schoolteachers, administrators, students' peers and family members, and the community at large. In the meantime, the evidence supports a need for continued implementation and development of Mental Illness Awareness Week programs like this for middle and high school students.

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# Transethnic Adoption and Personality Traits: A Lesson From Japanese Orphans Returned From China to Japan

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*The authors interviewed 25 Japanese who had been left as orphans in China at the end of World War II and who had recently returned to Japan with their Chinese spouses after almost four decades. It was found that even though they had been raised as Chinese culturally for almost their entire lives, most of these subjects had retained certain Japanese personality traits and social behavior from early childhood, and these characteristics distinguished them from their Chinese counterparts.*

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It has been estimated that more than 2,500 Japanese children left as orphans in China at the end of World War II were adopted and raised by Chinese foster parents (1). When the Russian army entered Manchuria (the northeastern part of China) shortly before the war ended in August 1945, the Japanese army had retreated to the border near Korea, leaving about 270,000 Japanese civilians, who had migrated to Manchuria, unprotected from the Russian army and from the rioting local Chinese (2). Many Chinese farmers who had been deprived of their land and suppressed by the Japanese army during the occupation of Manchuria reacted with vengeance toward the Japanese. Facing such circumstances, some Japanese attempted collective suicide, while the rest tried to retreat hurriedly in a group. The situation was worsened by the onset of winter, when many Japanese civilians suffered from extreme hunger, severe cold weather, and the threat of losing their lives (2).

During this terrible situation many small children were orphaned when their parents were killed, taken away by the army, or lost during the confusion of retreat. Some of the children who were sick or suffering from starvation were given by their parents to Chinese families, with the hope that the children would have a better chance of survival if they were cared for by the local Chinese while the adults continued their long and risky journey of retreat (3). Many childless Chinese couples were willing to adopt these children.

The Japanese war "orphans" lost the chance to recontact their families of origin because of the subsequent civil war in China and the discontinuation of diplomatic relations between China and Japan. Even though the relationship between the two countries returned to normal in 1972, the search for the Japanese orphans left behind in China did not become official and active until 1981—almost four decades after the war (1). By then the surviving Japanese orphans were middle-aged adults. They had been raised by their Chinese foster parents as Chinese and had Chinese spouses, and most of them were now themselves parents of teen-age children.

Starting in 1981, the Japanese government initiated a program to help the Japanese left in China to visit Japan and search for their biological families. Between 1981 and 1987 a total of 1,488 of these orphans visited Japan. Since the search for their families of origin relied mostly on memories of the situation in which the children had been separated, the older orphans had a better chance of finding their families. Of those who had been 9 years of age or older at the time of separation, 77.5% were to find their original families, while of those who had been between the ages of 6 and 8, only 47.5% were successful. Less than 31.3% of those younger than age 5 at the time of separation succeeded in finding their families (1).

Whether or not they found their relatives, the orphans were recognized as Japanese and were permitted to return to live in Japan if they so wished. As a result, many of these middle-aged Japanese orphans, accompanied by their Chinese spouses and children, have returned and settled in Japan or are on their way back.

This historical incident was a great human tragedy, yet it has provided a unique natural laboratory for

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examining human behavior, especially the effect of cross-ethnic or cross-cultural adoption. For this reason the present investigation was undertaken as a part of a larger research project. In this report, the major focus is the manifestation of ethnically related personality traits in association with transethnic adoption.

## METHOD

In preparation for developing a follow-up survey of the mental health adjustment of the Japanese orphans who returned to Japan from China, 25 families were interviewed while they were enrolled in the China Returned Orphans Settlement Promotion Center near metropolitan Tokyo. The center was established by the Ministry of Social Welfare of the Japanese government. All of the Japanese orphans and their Chinese spouses and teen-age children who left China and intended to settle in Japan were required to enter the center as soon as they arrived in Japan and spend 4 months in the settlement promotion program. The program focused on language training as well as guidance in adjusting to life in Japan.

In March 1988, with assistance from the center, 25 families were interviewed by the investigators, one of whom (W-S.T.) is bilingual in Chinese and Japanese. The purpose of the family interview was to understand the family history and background, the motives for moving to Japan, and the family members' reactions to their new cultural setting. The orphans' personal histories of separation from their families of origin, their childhood experiences as adoptees, and their adult personalities were also explored during the interviews.

## FINDINGS

Among the 25 orphans interviewed, ages ranged from 42 to 54 years, with a mean age of 46. Eleven (44%) were male, and 14 (56%) were female. Their educational backgrounds varied greatly: two (8%) were illiterate, nine (36%) had an elementary education, nine (36%) had attended middle school, and five (20%) had a college education.

Three (12%) of the orphans had been separated from their Japanese parents before the age of 1 year, five (20%) between ages 1 and 2, 13 (52%) between ages 3 and 5, and four (16%) between ages 6 and 8. Among the nine orphans who were under the age of 3 when the separation took place, all except one had no recollection of the separation. Those who were about 4 years old at the time had various degrees of recollection. If they were older than 5, they usually had some painful recollections, such as remembering that their mothers were taken away by Russian soldiers or that they cried for a long time after being given to the Chinese families by their parents. Recollection was strongly related to the age of the child at the time as well as to the circumstances of the separation.

Fourteen orphans who had no recollection of separation had begun to become aware of their Japanese heritage between the ages of 6 and 8, or about the time they entered grade school. Most were teased by neighborhood children or schoolmates as being "little Japanese." Since Japan was considered an enemy nation by China at that time, any person who had connections with Japan was considered unfavorably and even suspected of working as a spy for Japan and was usually maltreated as a result. In addition, since the Chinese culture tended to emphasize blood relationships and hold others—especially those with adopted Japanese—in disfavor, most Chinese foster parents tried to conceal the fact that their adopted children were Japanese. Knowing of their foster parents' concern, many orphans did not question the parents about the matter of their adoption. In several cases the orphans only learned of their adoption histories many years later, when their aged foster parents were sick and about to die. As an extension of this delicate situation, about one-half of the orphans had not revealed their Japanese heritage to their spouses before marriage.

Because the Japanese share the same Mongolian racial background as the Chinese and because the Japanese orphans had been reared as Chinese for most of their lives, it should have been difficult to recognize them as Japanese if one met them casually and they were with other Chinese. Before each family interview, the investigators examined a picture of the family that included the Japanese orphan and his or her Chinese spouse and tried to guess which person was the orphan. Even though all of the people in the photograph wore Chinese dress, most of the investigators were able to recognize the Japanese person 65% of the time—a higher rate than the 50% expected by chance, but not statistically significant ($p=0.23$). This guess was based purely on physiognomy.

At the beginning of the face-to-face interviews, the investigators also attempted to identify the Japanese partner within 30 seconds of meeting the couple for the first time, on the basis of a simple greeting. All of the couples were met by the investigators at the interview room of the Settlement Promotion Center. Since the couples had arrived in Japan within the past 3 months, they still wore the Chinese clothes they had brought with them. And since most of them hardly spoke Japanese, the greetings were carried out in Chinese when they entered the interview room. Surprisingly, the various investigators correctly identified 85% of the Japanese partners in the interview room, a highly significant percentage ($p=0.0009$). The grounds for identification varied among the investigators; some relied on physiognomic characteristics, while others depended on clues from facial expression, gestures, and manner. Usually, the Japanese partner tended to demonstrate more politeness, orderliness, and seriousness in his or her bodily expressions than the Chinese partner. These characteristics were more distinguishable among the female subjects, and were less obvious

**TABLE 1. Personality Traits of 25 Japanese Orphans as Described by Their Chinese Spouses**

| | Number of Subjects | | | | |
|---|---|---|---|---|---|
| | Sex of Orphan | | Age at Separation From Parents | | |
| Trait | Male (N=11) | Female (N=14) | 1–3 Years (N=11) | 4–8 Years (N=14) | Total (N=25) |
| Interpersonal relations | 5 | 15 | 1 | 19 | 20 |
| Polite/observes etiquette | 2 | 3 | 0 | 5 | 5 |
| Obedient/loyal to authority | 0 | 2 | 0 | 2 | 2 |
| Self-reliant/confident | 0 | 2 | 0 | 2 | 2 |
| Group oriented | 1 | 2 | 0 | 3 | 3 |
| Thoughtful/cooperative | 2 | 2 | 0 | 4 | 4 |
| Kind/obedient to husband | — | 2 | 1 | 1 | 2 |
| Filial respect toward parents | 0 | 1 | 0 | 1 | 1 |
| Severely disciplines children | 0 | 1 | 0 | 1 | 1 |
| Attitude toward work | 7 | 9 | 8 | 8 | 16 |
| Serious | 2 | 1 | 1 | 2 | 3 |
| Hard working | 0 | 2 | 1 | 1 | 2 |
| Responsible | 1 | 2 | 2 | 1 | 3 |
| Does things in orderly fashion | 3 | 0 | 1 | 2 | 3 |
| Takes initiative | 0 | 1 | 0 | 1 | 1 |
| Strives for achievement | 0 | 1 | 1 | 0 | 1 |
| Endures hardship | 1 | 2 | 2 | 1 | 3 |
| Temperament | 8 | 13 | 11 | 10 | 21 |
| Frank and honest | 1 | 2 | 0 | 3 | 3 |
| Reasonable/wise | 1 | 2 | 2 | 1 | 3 |
| Passionate | 0 | 1 | 0 | 1 | 1 |
| Acts fast/impulsive | 2 | 5 | 5 | 2 | 7 |
| Persistent | 3 | 2 | 3 | 2 | 5 |
| Has a temper | 1 | 1 | 1 | 1 | 2 |
| Habits/manners | 6 | 16 | 11 | 11 | 22 |
| Likes to be clean | 1 | 9 | 4 | 6 | 10 |
| Sits down by kneeling | 0 | 1 | 1 | 0 | 1 |
| Bows deeply | 1 | 0 | 0 | 1 | 1 |
| Fond of sweets | 4 | 6 | 6 | 4 | 10 |

in some of the male subjects, particularly those who were farmers or laborers.

### *Description of Personality Characteristics*

As part of the interview, all of the Chinese spouses were asked whether, at the time of marriage, they had noticed any personal characteristics about their (Japanese) spouses that were different from those of Chinese adults of the same gender. Twenty-one (84%) of the 25 spouses replied that they had. The descriptions of the personal characteristics given by the Chinese spouses were compiled, and a summation is presented in table 1.

The traits endorsed by the Chinese spouses of the Japanese individuals were clustered into four groups: interpersonal relations, attitude toward work, temperament, and habits/manners, as seen in table 1. For each of these clusters, the individual traits were scored as 1 for present or 0 for absent for each subject. These 1 or 0 ratings were then summed for each individual for each cluster of traits. For example, of a subject had two traits attributed to him that reflected interpersonal relations, his score was 2 in that cluster. These summed scores were then subjected to an analysis of variance to determine whether there were any sex differences, any differences according to age at separation (1–3 years versus 4–8 years), and any interactions between sex and age at separation. Table 2 shows the mean numbers of traits in the four clusters overall by sex, age at separation, and age-sex categories.

The only statistically significant difference we found was for interpersonal relations. Female subjects and those who were 4–8 years old at separation had significantly more traits reflecting interpersonal relations. There was no significant Sex by Age interaction. Fifty-three percent of the variance on the interpersonal relations variable was explained by the demographic categories. Twelve percent, 6%, and 14% percent of the attitude toward work, temperament, and habits/manners variables, respectively, was explained by the demographic variables. These analyses have some interesting implications for the effects of early childhood experiences on later behavior. The data suggest that experiences which occur before a child is 3 years old may not influence interpersonal relations as greatly as commonly believed.

Several additional findings emerged from these interviews. The four spouses who replied that their (Japanese) spouses did not have any distinguishable characteristics were wives of farmers or laborers. This suggests that the male subjects of the laboring class retained fewer distinguishable Japanese characteristics.

It is interesting to note that 10 of the 25 Japanese

**TABLE 2. Relation Between Demographic Variables and Personality Traits of 25 Japanese Orphans**

| | Number of Traits in Cluster | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | Interpersonal Relations[a] | | Attitude Toward Work | | Temperament | | Habits/Manners | |
| Demographic Variable | Mean | SD | Mean | SD | Mean | SD | Mean | SD |
| Total | 0.80 | 1.00 | 0.64 | 0.81 | 0.84 | 0.80 | 0.88 | 0.88 |
| Sex | | | | | | | | |
| Male | 0.46 | 0.82 | 0.64 | 0.67 | 0.73 | 0.79 | 0.55 | 0.82 |
| Female | 1.07[b] | 1.07 | 0.64 | 0.93 | 0.93 | 0.83 | 1.14 | 0.86 |
| Age at separation from parents | | | | | | | | |
| 1–3 years | 0.09 | 0.30 | 0.73 | 0.91 | 1.00 | 0.77 | 1.00 | 1.00 |
| 4–8 years | 1.36[b] | 1.01 | 0.57 | 0.76 | 0.71 | 0.83 | 0.79 | 0.80 |
| Interaction of sex and age at separation | | | | | | | | |
| Male × 1–3 years | 0.00 | 0.00 | 0.40 | 0.55 | 1.00 | 1.00 | 0.60 | 0.89 |
| Female × 1–3 years | 0.17 | 0.41 | 1.00 | 1.10 | 1.00 | 0.63 | 1.33 | 1.03 |
| Male × 4–8 years | 0.83 | 0.98 | 0.83 | 0.75 | 0.50 | 0.55 | 0.50 | 0.84 |
| Female × 4–8 years | 1.75 | 0.89 | 0.38 | 0.74 | 0.88 | 0.99 | 1.00 | 0.76 |

[a] $R^2=0.53$, $p=0.0009$.
[b] $p<0.05$.

subjects were described as liking to be clean more than the average Chinese person (taking more frequent baths, doing more laundry, or cleaning the house more often). Nine of these 10 were female. There were also some interesting findings regarding behavioral habits/manners. One subject was described this way by her husband: "Even now, she sits down on the bed by kneeling"—a Japanese mannerism that was never adopted by the Chinese. One wife reported that in the past, she had wondered why her husband would make a deep bow in greeting. Before she discovered that he was actually Japanese, she had thought that he needed to bend at the waist because he was so tall.

An unexpected finding was that in contrast to the Chinese in general, 40% (N=10) of the Japanese subjects were reported to be particularly fond of sweets. They added sugar to bread, mixed sugar in their rice, or preferred very sweet desserts—eating habits that are not characteristic of the Chinese.

## DISCUSSION

The subject of adoption across racial or ethnic groups has recently attracted interest among social and behavioral scientists and mental health professionals and has been explored from various perspectives: the genetic factor involved in racial differences (4), the psychological aspects of adoption (5, 6), cultural and ethnic identity (7), and the search for and reunion with birth parents (8, 9). Possible psychiatric effects have also been reviewed and investigated (10–12).

Concerning the effect of personality formation, Loehlin et al. (13) investigated 300 adoptive families using age-appropriate versions of Cattell's personality scales and reported that there was little personality resemblance among family members, whether they were biologically or adoptively related. Similar results were obtained later when these authors (14) used the California Psychological Inventory and the Thurstone Temperament Schedule to survey 220 families with adopted children. They reported that there was very little resemblance between parents and adopted children, and they interpreted this finding as showing that much of the explanation for personality variation must lie in within-family environmental variation or nonadditive genetic effects. These two surveys, undertaken in Texas, were mainly concerned with adoption within the same ethnic group. To our knowledge, there have been no studies of adoption that takes place across racial or ethnic groups. Also, the two investigations by Loehlin et al. were focused on adoptees who were still children or teen-agers; no investigation was undertaken after the adoptees had reached adulthood.

Guilford (15) has specified four groups or "modalities" of personality traits: somatic, motivational, aptitude, and temperament. Motivational traits are further subcategorized into needs, attitudes, and interests. Temperament refers to the manner in which behavior occurs. The complexity of personality structure can be perceived according to multidimensional, hierarchical, or matrix models. Among cross-culturally oriented behavior scientists, the terms "social character," "modal personality," and "basic personality" have been used to describe common features of personality traits shared by an ethnic or cultural group (16).

The characteristics of Japanese personality have been investigated and described by many scholars. For example, Doi (17), on the basis of clinical insight, emphasized *amae* (dependency) as a key concept for understanding Japanese personality structure. Lebra (18), a social scientist, listed numerous behavior orientations, such as social preoccupation, collectivism, conformism, empathy, and reciprocity, among others, as part of the Japanese pattern of behavior. Similarly, the characteristics of Chinese personality have been elaborated intuitively or investigated empirically by numerous behavioral scientists (19, 20). All of the empirical investigations have been extensively reviewed by Yang (21). Most of them were oriented toward comparisons with Western populations (mainly American). There are no earlier studies that focus on the direct comparison of personality in Japanese and Chinese groups. Since by definition the personality characteristics of any group are unique in reference to those of others, the traits or characteristics will vary theoretically depending on the groups being compared.

Our study shows that the special characteristics of the Japanese orphans were perceived and described by their Chinese spouses. The spouses' descriptions, even though subjective in nature, reflected the possible differences in social characteristics between the Japanese orphans and their Chinese counterparts. Among the characteristics of personality described, some might be attributed to the life experience of adoption. As pointed out by Smith (6), certain coping behavior patterns may be associated with the experience of early separation from the parents or of being discriminated against by others (as "little Japanese," in this case). However, a review of the personality traits mentioned by the spouses reveals that most can be matched with the traits that we have described as characteristic of the Japanese character in general (in contrast to the Chinese). Therefore, there are good reasons to assume that most of the traits described by the spouses were closely related to the orphans' Japanese backgrounds, even though they had been separated from their Japanese families of origin at an early age.

It can be speculated further that behavior relating to interpersonal relations, or social behavior, is formed at a later stage of childhood. Thus, subjects who were separated from their Japanese parents before the age of 3 were less likely to retain characteristic Japanese social or interpersonal behavior. In contrast, temperament is developed at an earlier stage of childhood or, perhaps, is closely related to hereditary predisposition, so the retention of personality traits in the form of temperament was more characteristic of the subjects who had experienced separation at an earlier age.

Associated with these interpretations is the matter of taste preference. From the point of view of developmental physiology, we know that the fixation of taste sensation occurs quite early in life, around the neonatal period, and that it is not subject to change. Our interviews indicated that toward the end of World War II, there was an extreme shortage of food for many Japanese, including those in Manchuria. Under such circumstances sugar was considered to be precious, and many Japanese families may have reserved it to dole out only to small children. This may help explain why these orphans had a taste for sweets.

In summary, from this unique experience of transethnic adoption, we found that Japanese orphans who had lived as Chinese for most of their lives grew up as Chinese in many respects, including language, lifestyle, and social adjustment, and became almost indistinguishable from Chinese people. However, through closer and careful examination we found that, in addition to their physiognomic features, most of them had retained certain Japanese facial expressions, gestures, and mannerisms that allowed them to be distinguished from their Chinese counterparts rather easily and accurately (better than they would be by chance) by the biculturally oriented investigators.

Furthermore, reports from their spouses disclosed that many of these subjects manifest certain personal characteristics that seem to be related to Japanese personality traits they have had since early childhood. Among those characteristics are traits related to social behavior, which were found mostly in those who were separated from their Japanese families after the age of 3 and which were more prevalent among females. Other traits related to temperament, attitude toward work, and taste preference seem to be less related to social experience.

From this aftermath of transethnic adoption, further investigations can be carried out to explore the issue of how ethnic and cultural factors, interacting with hereditary factors and life experiences, may mold the formation of personality traits.

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# Sexual Assault and Psychiatric Disorders Among a Community Sample of Women

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*The authors examined the relationships between sexual assault and psychiatric disorders in a sample of 1,157 women 18–64 years old in the North Carolina site of the NIMH Epidemiologic Catchment Area Program. The results suggest that sexual assault is a risk factor for a number of psychiatric disorders. In addition, several characteristics of the assault among sexual assault victims were significantly related to one or more psychiatric disorders. However, there was no clear pattern relating characteristics of the assault to the risk of specific psychiatric disorders.*

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There is growing evidence in the research literature that rape and other forms of sexual assault usually lead to short-term psychological problems for victims. Victims of sexual assault exhibit more psychiatric symptoms (especially symptoms of depression, anxiety, somatization, obsessive-compulsive disorder, and paranoid ideation) than nonvictims (1–4), more fear and negative mood states (2), and poorer social adjustment (5). Most previous studies examined symptoms from a relatively narrow range of psychiatric disorders. There remains a need to examine a broader range of diagnostic categories in order to assess the strength and diversity of the link between sexual assault and psychiatric morbidity.

Some empirical studies have examined the long-term effects of sexual assault (6–12). Although the proportions differ across studies, the majority of the evidence suggests that most sexual assault victims "recover" in the sense that they recover from their psychological problems and regain adequate levels of social adjustment (13). Many clinical reports, however, have reported that sexual assault, particularly forcible rape and assault at an early age, leaves permanent psychological damage (11, 14, 15). Several have also reported that a history of previous problems predicts the severity of response to and difficulty in recovery from sexual assault: persons with lower levels of functioning before the assault are at greater risk for long-term psychiatric problems (3, 7, 9, 14, 16–20).

Another important research issue, then, is identification of the factors that predict differential outcomes of sexual assault (i.e., long-term adjustment problems versus recovery). In addition to level of functioning before the assault, a number of previous studies examined the degree to which characteristics of the sexual assault affect psychiatric outcomes. Unfortunately, there is little consistency in the findings of these studies. In part, this inconsistency reflects the fact that investigators do not agree on a set of assault characteristics potentially relevant to the outcomes of interest.

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Beyond that, however, there are obvious contradictions across studies. Becker et al. (4) examined numerous characteristics of sexual assaults, including number of assaults, type of assault, time since most recent assault, whether the assailant was a stranger, location of the assault, level of aggression used by the assailant, whether penetration occurred, whether a weapon was used, and whether the assault was reported to the police. Of these, only use of a weapon was significantly related to levels of depression in the victim. In another study of sexual trauma, Ruch and Chandler (19) examined the impact of a variety of assault characteristics—number of assailants, victim's relationship to assailant, location of assault, use of verbal threats, use of physical force, use of weapon, resistance by the victim, and injury to the victim. Three of these characteristics—number of assailants, victim's relationship to assailant, and injury to the victim—were significantly correlated with amount of trauma. Even these relationships were quite modest, however, since the three variables combined explained only 2% of the variance in the measure of sexual assault trauma. Ruch and Chandler (19) also reported that victims reporting their first sexual assault exhibited higher levels of trauma than victims who had previously been sexually abused. Taken together, these findings do not suggest that characteristics of the sexual assault have strong effects on the impact of the assault, but considerably more evidence is needed to clarify the relationship between the characteristics of a sexual assault and the long-term consequences of sexual abuse.

In this paper, we examine the relationships between sexual assault and psychiatric disorders, including the timing of the first onset of psychiatric disorder, in a random community sample. We also examine the degree to which characteristics of the sexual assault affected the victims' psychiatric outcomes.

## METHOD

### *Sample*

Our data come from the National Institute of Mental Health (NIMH) Epidemiologic Catchment Area Program. Five sites geographically distributed throughout the United States (New Haven, East Baltimore, St. Louis, the Piedmont of North Carolina, and East Los Angeles) were each randomly sampled to yield approximately 3,000 interviews.

In the Piedmont area health survey, all housing units in a five-county area in the north-central Piedmont of North Carolina were sampled. The segments were selected to be demographically representative of the population of the five counties in terms of race, rural versus urban residence, and socioeconomic status. Elderly residents were oversampled in all of the segments selected. For each household selected, all residents 18 years old and older were identified, and the Kish method (21) was used to select one potential participant from each household. For the elderly oversample, the same method was applied to select one potential participant 60 years of age or older.

Questions about sexual assault were included only in a second series of interviews, conducted 1 year after the initial interviews. Every effort was made to locate and interview all respondents in this second series. Interviews were completed with 77% of the respondents who had been interviewed in the first series. Attrition, however, should pose little threat to the validity of the analyses presented in this paper because of the use of appropriate sample weights. The original weights in the Epidemiologic Catchment Area database were designed to adjust for the presence of the elderly oversample, differential nonresponse among sample members, and differential probability of selection within households of different sizes. They were also designed to match the demographic profile of the five-county area in terms of age, race, sex, and rural versus urban residence (as generated by the U.S. Census Bureau). An additional weight was constructed after collection of the second series of data to adjust for differential nonresponse (other than mortality) among demographic subgroups. All of the statistical estimates reported here are based on weighted data, although we used the original sample size for testing statistical significance. In order to make our results comparable with previous studies, we examined a restricted sample of women 18–64 years old who were living in the community. We call this more restricted sample the Epidemiologic Catchment Area sexual assault sample. The total size of the sexual assault sample is 1,157.

Table 1 presents the demographic characteristics of the 1,157 respondents in the Epidemiologic Catchment Area sexual assault sample. The age distribution of the sample matched that of the five-county area, and most of the women were white, but there was a large proportion of blacks. The sample had a modal educational level of high school graduate, was about evenly distributed between rural and urban residents, and had a broad distribution on marital status.

From the perspective of research design, the quality of the Piedmont Epidemiologic Catchment Area sexual assault sample was superior to the sexual assault samples reported in most previous literature, which relied on recruitment of subjects through rape crisis centers and, to a lesser extent, media campaigns. Given the nature of those samples, it is difficult to determine whether the characteristics of research participants represented characteristics of service users and research volunteers or characteristics of sexual assault victims.

### *Measures of Psychiatric Disorders and Sexual Assault*

The NIMH Diagnostic Interview Schedule (DIS) (22) was administered to each participant in the survey. The DIS is a highly structured interview developed

**TABLE 1. Demographic Characteristics of the Epidemiologic Catchment Area Sexual Assault Sample of 1,157 Women**

| Characteristic | Unweighted N | Weighted % | SD | SE |
|---|---|---|---|---|
| Age (years) | | | | |
| 18–24 | 115 | 17.76 | 38.23 | 1.12 |
| 25–44 | 553 | 49.09 | 50.01 | 1.47 |
| 45–64 | 489 | 33.15 | 47.09 | 1.38 |
| Race[a] | | | 48.94 | 1.44 |
| White | 704 | 60.33 | | |
| Nonwhite | 453 | 39.67 | | |
| Education | | | | |
| Less than high school | 374 | 27.23 | 44.53 | 1.31 |
| High school graduate | 378 | 36.71 | 48.22 | 1.42 |
| Some college | 194 | 16.78 | 37.39 | 1.10 |
| College graduate | 211 | 19.28 | 39.46 | 1.16 |
| Place of residence[a] | | | 49.42 | 1.47 |
| Urban | 560 | 53.17 | | |
| Rural | 597 | 46.83 | | |
| Marital status | | | | |
| Married, living with spouse | 623 | 57.98 | 49.38 | 1.45 |
| Married, not living with spouse | 16 | 1.26 | 11.16 | 0.33 |
| Separated or divorced | 202 | 13.57 | 34.26 | 1.01 |
| Widowed | 141 | 6.46 | 24.59 | 0.72 |
| Never married | 175 | 20.73 | 40.56 | 1.19 |

[a]Dichotomous variable, yielding a single standard deviation and a single standard error.

for use by lay interviewers in epidemiologic studies. Computer-based diagnoses for selected *DSM-III* disorders can be generated by using the DIS. Moreover, age at onset is reported on the DIS, permitting examination of whether psychiatric illness preceded or followed the respondent's first sexual assault—a crucial issue when one is examining the lifetime prevalence of both psychiatric disorder and sexual assault. In this paper we report on the following *DSM-III*/DIS diagnoses: major depression, dysthymia, alcohol abuse or dependence, drug abuse or dependence, somatization, schizophrenia or schizophreniform disorder, generalized anxiety, panic disorder, posttraumatic stress disorder, and obsessive-compulsive disorder. The *DSM-III* exclusions hierarchy was not used, primarily because of its questionable validity (23). Thus, respondents may have had more than one diagnosis.

The second-series interviews included a detailed and relatively comprehensive battery of questions about sexual assault. The definition of sexual assault varies widely across studies. As Katz and Mazur (13) noted, failure to distinguish among types of sexual assault and failure to use consistent definitions of rape and other types of sexual assault seriously compromise cross-study comparisons. In this study, the presence of a sexual assault was determined by a positive response to the question, "Have you ever been in a situation in which you were pressured into doing more sexually than you wanted to do, that is, a situation in which someone pressured you against your will into forced contact with the sexual parts of your body or their body?" Information also was obtained about the respondent's history of sexual assault, characteristics of the sexual assault, how the sexual assault affected the respondent's life, and the sources of help that were used in dealing with the sexual assault.

Given the sensitivity of the topic, social desirability was an important source of potential bias. In order to minimize denial and social desirability, the sexual assault battery was placed near the end of the interview (after the DIS) under the assumption that rapport between interviewer and respondent would be maximized. In addition, the questions about sexual assault were asked by an interviewer of the same sex as the respondent. Despite these procedures, 12 respondents refused to answer questions about sexual assault. Although these 12 respondents represented only 1% of the sexual assault sample, this group merits further investigation because of the low prevalence of sexual assault found in the entire sample (5.9%). Analyses were performed to determine whether respondents who refused to answer the sexual assault questions differed systematically from other respondents. Respondents who refused to answer the sexual assault questions did not systematically differ in terms of demographic characteristics and psychiatric status from those who reported no sexual assault or from those who did report sexual assault. Respondents who refused to answer the sexual assault questions were demographically more similar to those who reported no sexual assault. With respect to psychiatric status, respondents who refused to answer the sexual assault questions had a higher prevalence of panic disorder and generalized anxiety disorder than either those who reported no sexual assault or those who did report sexual assault. The refusal group, however, did not significantly differ in psychiatric symptoms from those who did report sexual assault.

## RESULTS

Table 2 shows the relationship of demographic variables to the likelihood of having experienced sexual assault. Age was significantly related to the prevalence of sexual assault: more than 7% of the respondents 44 years old or younger reported being the victims of sexual assault, compared with 3% of those 45–64 years of age. These age differences appear to reflect historical trends in the occurrence of sexual assault that are in part a function of changes in sexual attitudes and women's life styles. These changes place younger women at greater risk of sexual assault and other kinds of criminal victimization.

There was a significant relationship between place of residence and the prevalence of sexual assault in this sample: the prevalence of sexual assault was higher among urban residents than among rural residents. The prevalence of sexual assault was also substantially higher among respondents with some college or more education than among those with a high school degree or those who never graduated from high school. Part

**TABLE 2. Relationships Between Sexual Assault and Demographic Variables Among 1,157 Women in the Epidemiologic Catchment Area Sexual Assault Sample**

| Characteristic | Weighted % Reporting Sexual Assault | SD | SE | $\chi^2$ | df | p |
|---|---|---|---|---|---|---|
| Age (years) | | | | 12.52 | 2 | 0.002 |
| 18–24 | 7.04 | 41.37 | 5.04 | | | |
| 25–44 | 7.44 | 48.71 | 5.93 | | | |
| 45–64 | 2.77 | 36.71 | 4.47 | | | |
| Race[a] | | 49.65 | 6.05 | 0.13 | 1 | 0.71 |
| White | 5.64 | | | | | |
| Nonwhite | 6.10 | | | | | |
| Education | | | | 6.1 | 3 | 0.10 |
| Less than high school | 3.65 | 50.09 | 6.10 | | | |
| High school graduate | 5.88 | 12.42 | 1.51 | | | |
| Some college | 7.95 | 35.82 | 4.36 | | | |
| College graduate | 6.94 | 21.84 | 2.66 | | | |
| Place of residence[a] | | 42.65 | 5.19 | 19.81 | 1 | 0.0001 |
| Urban | 8.37 | | | | | |
| Rural | 2.93 | | | | | |
| Marital status | | | | 0.92 | 4 | 0.92 |
| Married, living with spouse | 5.55 | 42.78 | 5.21 | | | |
| Married, not living with spouse | 7.13 | 37.90 | 4.62 | | | |
| Separated or divorced | 6.37 | 48.66 | 5.93 | | | |
| Widowed | 4.45 | 42.33 | 5.16 | | | |
| Never married | 6.57 | 42.38 | 5.16 | | | |

[a] Dichotomous variable, yielding a single standard deviation and a single standard error.

**TABLE 3. Relationships Between Sexual Assault and Lifetime *DSM-III* Disorders Among 1,157 Women in the Epidemiologic Catchment Area Sexual Assault Sample**

| | Sexual Assault Reported | | | Sexual Assault Not Reported | | | | |
|---|---|---|---|---|---|---|---|---|
| Disorder | Weighted % | SD | SE | Weighted % | SD | SE | $\chi^2$ (df=1) | p |
| Major depression | 12.93 | 33.81 | 4.12 | 5.78 | 23.35 | 0.71 | 5.58 | 0.02 |
| Dysthymia | 3.95 | 19.62 | 2.39 | 4.14 | 19.93 | 0.60 | 0.01 | 0.94 |
| Alcohol abuse or dependence | 7.17 | 25.99 | 3.17 | 1.98 | 13.94 | 0.42 | 7.65 | 0.01 |
| Drug abuse or dependence | 3.81 | 19.28 | 2.35 | 0.90 | 9.43 | 0.29 | 5.09 | 0.02 |
| Somatization disorder | 0.0 | 0.0 | 0.0 | 0.51 | 7.13 | 0.22 | 0.35 | 0.56 |
| Schizophrenia or schizophreniform disorder | 0.0 | 0.0 | 0.0 | 0.84 | 9.12 | 0.28 | 0.57 | 0.45 |
| Generalized anxiety disorder | 11.99 | 32.73 | 3.99 | 9.15 | 28.85 | 0.87 | 0.61 | 0.44 |
| Panic disorder | 3.30 | 17.99 | 2.19 | 0.78 | 8.80 | 0.27 | 4.38 | 0.04 |
| Posttraumatic stress disorder | 3.66 | 18.92 | 2.31 | 0.89 | 9.38 | 0.28 | 4.71 | 0.03 |
| Obsessive-compulsive disorder | 6.97 | 25.65 | 3.12 | 2.15 | 14.51 | 0.44 | 6.21 | 0.01 |

of the reason for these relationships may be that younger women and urban residents were better educated.

There was no significant racial difference in the likelihood of experiencing sexual assault in this sample. The prevalence of sexual assault varied by marital status, but the differences were not statistically significant. Widowed respondents reported a lower prevalence of sexual assault than women in the other four marital status categories. The low prevalence among widowed respondents reflected age differences in marital status.

Table 3 presents the prevalences of 10 lifetime *DSM-III*/DIS disorders among respondents with and without histories of sexual assault. The 10 disorders were selected because they represent the psychiatric disorders and types of symptoms examined in most previous studies (2, 20). It should be noted that both psychiatric disorders and sexual assault were measured in terms of lifetime occurrence and that temporal order is not taken into account. As the table indicates, six of the 10 disorders were significantly related to sexual assault. Sexual assault was not significantly related to dysthymia, somatization disorder, schizophrenia or schizophreniform disorder, or generalized anxiety,. Somatization disorder and schizophrenia or schizophreniform disorder, however, were very rare in the sample as a

**TABLE 4. Relationship Between Age at First Sexual Assault and Age at Onset of *DSM-III*/DIS Disorders Among 60 Women in the Epidemiologic Catchment Area Sexual Assault Sample**

| Diagnosis | Onset Before First Sexual Assault (weighted %) | Onset After First Sexual Assault (weighted %) | Onset at Same Time as First Sexual Assault (weighted %) |
|---|---|---|---|
| Major depression | 3.80 | 96.20 | 0.00 |
| Single episode | 0.00 | 100.00 | 0.00 |
| Recurrent depression | 4.80 | 95.20 | 0.00 |
| Alcohol abuse or dependence | 0.00 | 100.00 | 0.00 |
| Drug abuse or dependence | 0.00 | 40.53 | 59.47 |
| Panic disorder | 100.00 | 0.00 | 0.00 |
| Obsessive-compulsive disorder | 45.61 | 54.39 | 0.00 |
| Generalized anxiety disorder | 9.04 | 90.96 | 0.00 |

whole. Consequently, our estimates for these diagnoses may be unstable.

The data in table 3 address the strength and diversity of the association between sexual assault and psychiatric disorders. Six of the 10 disorders were significantly more prevalent among sexual assault victims than among nonvictims—a pattern that supports the view that sexual assault is a generalized risk factor. However, the magnitude of the relative risk posed by sexual assault was considerably larger for some diagnoses than for others. The data in table 3 suggest that sexual assault was most strongly associated with five of the 10 disorders: alcohol abuse or dependence, drug abuse or dependence, panic disorder, posttraumatic stress disorder, and obsessive-compulsive disorder. These findings lend at least partial support for the view that sexual assault is a risk factor for specific types of psychiatric morbidity.

As noted earlier, the relationships in table 3 ignore temporal order. The Epidemiologic Catchment Area data, however, provide an opportunity to examine the self-reported timing of the onset of psychiatric disorder in relation to self-reported age at first sexual assault. Cross-classifying age at onset of psychiatric illness by age at the first assault generates three possible categories: onset of psychiatric illness before first sexual assault, onset of psychiatric illness after first sexual assault, and onset of psychiatric illness at the same time as sexual assault. As is standard with the DIS (22), age at onset is established as the age at which the first symptom of a disorder appeared.

Table 4 shows the relationship between age at onset of psychiatric disorder and age at the time of sexual assault for the sexual assault victims who also met criteria for one or more *DSM-III*/DIS disorders. We examined the sequence patterns for eight disorders, including single depressive episode versus recurrent depression. Information was not available on age at onset for dysthymia and posttraumatic stress disorder. Also, as reported in table 3, none of the respondents reporting sexual assault met the criteria for a diagnosis of somatization disorder or schizophrenia or schizophreniform disorder. Even with the use of weighted data, the numbers in the rows of the table are small. Nonetheless, it is useful to examine the temporal patterns exhibited in the data. For seven of the eight diagnoses presented in table 4, half or more of the sexual assault victims experienced onset of those disorders at about the same time as or after their first sexual assault. Only for panic disorder did a majority of the sexual assault victims report onset of the psychiatric disorder before the first sexual assault. For the sample as a whole, then, the primary direction of self-reported temporal order was for sexual assault to occur before or at the same time as the onset of psychiatric problems. Moreover, a majority of the sexual assault victims who reported onset of psychiatric disorder before their first sexual assault also reported episodes of psychiatric disorder after their sexual assault.

As noted earlier, some of the greatest inconsistencies in the sexual assault literature concern the impact of different characteristics of sexual assault on the relationships between sexual assault and subsequent mental health. These data provide the opportunity to examine many characteristics of sexual assault as mediators of the relationships between sexual assault and psychiatric disorders. Because of the multiple psychiatric disorders and characteristics of sexual assault examined, table 5 presents results only for the significant relationships found. These analyses are based on the 60 respondents with histories of sexual assault. Within this group, we compared respondents with and without the sexual assault characteristic under consideration to determine whether the characteristic of sexual assault significantly related to psychiatric disorders.

Table 5 lists the six characteristics of sexual assault that were significantly related to one or more lifetime psychiatric diagnoses. Five characteristics of the sexual assault were not significantly related to any type of psychiatric disorder; these are listed in the footnote to table 5. There is little pattern to the findings—either with regard to the specific disorders affected by characteristics of the sexual assault or the types of characteristics of sexual assault most likely to lead to vulnerability to psychiatric morbidity. Nevertheless, it is not surprising to see that posttraumatic stress disorder was associated with sexual assault that involved physical injury.

## DISCUSSION

This study examined the relationships between sexual assault and psychiatric disorders as well as the extent to which characteristics of the sexual assault affected these relationships. Our findings suggest that sexual assault is a risk factor for a number of psychiatric disorders but more so for some than for others. It is difficult to assess the consistency of this finding, be-

**TABLE 5. Significant Relationships Between *DSM-III*/DIS Disorders and Characteristics of Sexual Assaults Among 60 Women in the Epidemiologic Catchment Area Sexual Assault Sample**

| Characteristic and Diagnosis[a] | Characteristic Reported | | | Characteristic Not Reported | | | $\chi^2$ | |
|---|---|---|---|---|---|---|---|---|
| | Weighted % | SD | SE | Weighted % | SD | SE | (df=1) | p |
| Assaulted more than once | | | | | | | | |
| Dysthymia | 11.18 | 32.19 | 6.60 | 0.00 | 0.00 | 0.00 | 4.41 | 0.04 |
| Generalized anxiety disorder | 29.37 | 46.53 | 9.54 | 2.89 | 16.98 | 2.76 | 8.97 | 0.00 |
| Obsessive-compulsive disorder | 15.43 | 36.90 | 7.56 | 2.71 | 16.46 | 2.68 | 3.35 | 0.07 |
| Pressured by verbal persuasion | | | | | | | | |
| Posttraumatic stress disorder | 0.00 | 0.00 | 0.00 | 7.81 | 27.27 | 4.85 | 2.85 | 0.09 |
| Obsessive-compulsive disorder | 12.42 | 33.46 | 5.64 | 1.05 | 10.36 | 1.84 | 3.28 | 0.07 |
| Pressured because assailant was stronger | | | | | | | | |
| Drug abuse or dependence | 1.69 | 13.01 | 1.66 | 28.61 | 50.13 | 21.71 | 9.61 | 0.00 |
| Dysthymia | 2.51 | 15.78 | 2.01 | 20.94 | 45.14 | 19.55 | 4.35 | 0.04 |
| Experienced physical injury | | | | | | | | |
| Posttraumatic stress disorder | 14.16 | 36.08 | 9.29 | 0.64 | 8.06 | 1.12 | 5.99 | 0.01 |
| Threatened with weapon | | | | | | | | |
| Alcohol abuse or dependence | 20.75 | 42.59 | 13.01 | 4.66 | 21.26 | 2.84 | 3.47 | 0.06 |
| Verbal threats of harm | | | | | | | | |
| Obsessive-compulsive disorder | 0.00 | 0.00 | 0.00 | 11.85 | 32.73 | 5.20 | 3.45 | 0.06 |

[a] The following characteristics were not significantly related to any psychiatric disorder: assault by a stranger (versus someone known to the respondent), drugged or gotten drunk by assailant, experience of physical restraint or violence, assault before age 16, and other pressures (i.e., other than by verbal persuasion and because assailant was stronger).

cause other investigators have not examined the association between specific psychiatric disorders and sexual assault in community samples. Our findings are somewhat consistent with those of Frank and Anderson (20), who reported that recent rape victims at a rape crisis center were significantly more likely than nonvictims to meet *DSM-III* criteria for current major depression and drug abuse diagnoses. They found no difference between the two groups in either generalized anxiety or alcohol abuse, however.

The impact of characteristics of sexual assault on subsequent mental health remains unclear. In this study, a wide range of psychiatric disorders were available for analysis. The Epidemiologic Catchment Area interview included a large number of characteristics of sexual assault, such as childhood versus adult sexual assault, number of sexual assaults, and the types of pressure used to generate compliance during the sexual assault. One of the limitations that we faced in examining this issue was the small number of women who had been victims of sexual assault. It is likely that this limitation precludes stable estimates of the relationships between characteristics of sexual assault and psychiatric outcomes. In addition, because of the small number of victims, extremely large differences were required for the results to achieve statistical significance. This topic merits further study, but it is obvious that a very large sample will be required to advance our understanding of this issue.

One of the possible limitations of using lifetime diagnoses of psychiatric disorders is the problem of recall. If the respondents with psychiatric disorders and sexual assault experiences were more likely to recall both sexual assault and their psychiatric symptoms, then there was nonrandom error in the data. Such nonrandom error may bias estimates of the relationship between sexual assault and psychiatric disorder. If we had found the same patterns of association between sexual assault and the multiple psychiatric disorders examined, this might suggest such systematic bias. Problems in recall did not appear to bias the results systematically because 1) some *DSM-III*/DIS disorders were significantly related to sexual assault but others were not and 2) for most disorders, sexual assault was reported to precede the onset of psychiatric morbidity, but that was not the pattern for panic disorder.

Our confidence in the findings based on lifetime diagnoses was increased by the fact that we were examining relationships rather than making prevalence estimates. Although the concordance of the DIS with diagnosis by psychiatrists has been found to be low to moderate, specificity has been found to be quite high (24, 25). Specificity is more important than sensitivity when examining the association between a disorder and a possible risk factor (26).

A strength of this study is its ability to provide estimates of the relationships between sexual assault and mental health outcomes by using data from a representative community sample. Also, the use of the DIS is a substantial advance over the mental health measures used in most previous studies. The DIS, unlike these other measures, is designed to operationalize the diagnostic criteria of standard psychiatric practice. In addition, the DIS generates information about a broad variety of psychiatric disorders, whereas most previous research was limited to examination of depression and/or anxiety symptoms. Although the analyses in this paper were restricted to *DSM-III*/DIS diagnoses, subsequent work will examine the associations of symptoms and configurations of symptoms with sexual assault.

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# Guns and Suicide: Possible Effects of Some Specific Legislation

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*The authors describe suicide rates in Toronto and Ontario and methods used for suicide in Toronto for 5 years before and after enactment of Canadian gun control legislation in 1978. They also present data from San Diego, Calif., where state laws attempt to limit access to guns by certain psychiatric patients. Both sets of data indicate that gun control legislation may have led to decreased use of guns by suicidal men, but the difference was apparently offset by an increase in suicide by leaping. In the case of men using guns for suicide, these data support a hypothesis of substitution of suicide method.*

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Stengel predicted as early as 1964 that restriction of guns would lead to a compensatory rise in suicide by drugs but possibly also a lowering of the overall rate (1). Browning suggested in 1974, "The only real test of the usefulness of such a program would be in its actual implementation over a period of time (5 or 10 years) . . . " (2).

In 1978, changes in the Criminal Code of Canada were implemented to provide tighter restriction on the ownership of guns by all citizens. Handguns were virtually forbidden. Further restrictions were made for persons with previous convictions or psychiatric histories that suggested a potential for violence. A nationwide educational program was conducted concerning the safe and secure use and storage of guns. Finally, persons who possessed unregistered guns were required to present them for registration or surrender. We report here on suicide rates for the 5 years before and after 1978 in Ontario and the city of Toronto. We describe the use of guns as a suicide method in Toronto during the same periods.

California also has a limited gun control law; it was initially passed in 1965 and implemented in 1969 (3). It prohibits possession of guns by any person "who is a mental patient in any hospital or institution or on leave of absence from any hospital or institution . . . . " Any person who "has been adjudicated to be a danger to others as a result of mental disorder or mental illness" is similarly prohibited from possessing any guns. The statutes stipulate penalties for anyone who provides such a patient with a gun. It requires confiscation of guns from such patients as well as from any person "who has been detained or apprehended for examination of his or her mental condition . . . . " Finally, it requires hospitals to report such persons to the State Department of Mental Health, which, in turn, reports to the Department of Justice when such information is requested. We also present here data on suicide methods from the large suicide investigation conducted in San Diego between 1981 and 1983.

## METHOD

For the purposes of consistency in this paper, the word "gun" is used to refer to all firearms. The population statistics and numbers of suicides for Ontario and Toronto and the methods of suicide for Toronto were taken from the records of the Office of the Chief Coroner for Ontario. All sudden or unexpected deaths (approximately 40% of all deaths) in Ontario are reported through the coroner system. They are ultimately categorized by the chief coroner's office as due to accident, homicide, suicide, natural causes, or undetermined causes. This, then, becomes the cause of death on the death certificate. All of the suicides in Toronto during the period of study were examined by one of the investigators (J.W.).

The mean values for the 5 years before 1978 (1973–1977) were compared to values for the 5 years afterward (1979–1983). Because the collection of guns was

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**TABLE 1. Suicide Rates in Metropolitan Toronto During 1973–1977 and 1979–1983**

| Year | Number of Suicides | Male-Female Ratio | Population | Suicide Rate[a] |
|---|---|---|---|---|
| 1973 | 298 | 1.71 | 2,079,004 | 14.3 |
| 1974 | 329 | 2.02 | 2,093,292 | 15.7 |
| 1975 | 319 | 1.73 | 2,232,700 | 14.3 |
| 1976 | 325 | 1.60 | 2,105,569 | 15.4 |
| 1977 | 370 | 1.82 | 2,107,128 | 17.6 |
| 1979 | 307 | 1.92 | 2,138,352 | 14.4 |
| 1980 | 332 | 2.02 | 2,142,556 | 15.5 |
| 1981 | 299 | 1.90 | 2,110,973 | 14.2 |
| 1982 | 337 | 2.18 | 2,140,347 | 15.7 |
| 1983 | 320 | 1.99 | 2,207,918 | 14.5 |

[a] Suicides per 100,000 population. The mean±SE suicide rates for 1973–1977 and 1979–1983 were 15.5±0.4 and 14.9±0.4. The difference between the mean rates for 1973–1977 and 1979–1983 was 0.6 (3.9%); the standard error of the difference was 0.5 ($t=1.14$, $df>2\times10^7$, $p=0.30$).

**TABLE 2. Suicide Methods Used by Men in Metropolitan Toronto During 1973–1977 and 1979–1983**

| Year | Number of Male Suicides | Mean Percentage of Male Suicides[a] | | |
|---|---|---|---|---|
| | | Shooting | Leaping | All Immediately Fatal Methods[b] |
| 1973 | 188 | 20 | 16 | 59 |
| 1974 | 220 | 21 | 16 | 62 |
| 1975 | 202 | 29 | 19 | 68 |
| 1976 | 200 | 25 | 14 | 60 |
| 1977 | 239 | 22 | 15 | 55 |
| 1979 | 202 | 16 | 18 | 53 |
| 1980 | 222 | 12 | 22 | 56 |
| 1981 | 196 | 15 | 22 | 64 |
| 1982 | 231 | 14 | 25 | 62 |
| 1983 | 213 | 23 | 24 | 68 |

[a] The mean±SE percentages of male suicides for 1973–1977 for shooting, leaping, and all immediately fatal methods were 23.2%±1.3%, 15.7%±1.1%, and 60.8%±1.5%; corresponding figures for 1979–1983 were 16.2%±1.1%, 22.5%±1.3%, and 60.7%±1.5%. The differences in mean percents for shooting, leaping, and all immediately fatal methods were 7.0%, 6.8%, and 0.1%; the standard errors of the differences were 1.7, 1.7, and 2.1, respectively ($t=4.1$, $df=2111$, $p<0.001$; $t=4.0$, $df=2111$, $p<0.001$; and $t=0.05$, $df=2111$, $p=0.96$).

[b] Shooting, leaping, hanging, electrocution, immolation, or automobile wrecks.

conducted throughout 1978, that year was excluded from the comparisons. The mean annual raw suicide rates in Ontario and Toronto and the mean proportions of all male suicides committed by guns and leaping that occurred in Toronto before and after 1978 were compared by using combined weighted values for all 5 years in each sample. Proportions of methods for suicides by men, rather than raw rates, were used because accurate sex breakdown of population figures was not available. It was assumed that no major changes in sex distribution of the Toronto population occurred during the periods studied. The stability of the male/female suicide ratio during those periods (table 1) supports that assumption. The t statistics were calculated by using 95% confidence intervals. Time series analyses were also performed to check for evidence of serially autocorrelated errors and within-period linear effects of time; these analyses used the Durbin-Watson test (4).

The San Diego suicide study was an investigation of 283 suicides that occurred between November 1981 and June 1983 in San Diego County, Calif. The methodology of the study has been described extensively elsewhere (5). Three groups of the subjects were used for comparison: 1) 133 consecutive subjects under age 30, 2) 150 consecutive subjects over age 30, and 3) an overlapping group of the first 204 subjects, without regard for age. In each case, the method of suicide was taken from the coroner's final report.

Information on whether or not subjects had received psychiatric treatment and whether or not they had owned a gun was not available for all cases. The number of subjects who were known to have received inpatient psychiatric treatment some time before their death was compared to those who were known to have received no treatment; Fisher's exact test was used in this comparison. In addition, the same treatment factors were used to compare those who were known to have owned guns to those who were known not to have owned guns; Fisher's exact test was also used in this comparison.

## RESULTS

The annual raw suicide rates for Toronto are shown in table 1. The rates were not adjusted for age, sex, or race, since there were no substantial shifts in the demographic patterns during this time period. In addition, the Durbin-Watson statistic indicated no evidence of serially autocorrelated errors. There was no statistically significant change in the mean total suicide rates for Toronto between the 5 years before and the 5 years after 1978 (table 1). Additional time series analysis initially suggested a slightly significant decrease in suicide rate from before 1978 to afterward ($t=2.06$, $df>2\times10^7$, $p=0.04$). This proved to be entirely due to the high 1977 rate. Rerunning the time series analysis and excluding 1977 revealed no evidence of any difference from before 1978 to afterward ($t=0.451$, $df>2\times10^7$, $p=0.65$). There was also no significant difference between the 5-year pre- and post-1978 mean±SE suicide rates for all of Ontario (15.6±0.2 versus 15.2±0.2) ($t=1.50$, $df>8\times10^7$, $p=0.13$).

There was a significant decrease in the mean proportion of suicides by shooting for the men in Toronto (table 2). There was also a significant increase in the mean proportion of men who committed suicide by leaping. There was no evidence of autocorrelated errors, and time series analysis did not alter the significance of these findings. There was no change over time in the mean proportion of Toronto men who used

**TABLE 3. Relationship of Psychiatric Treatment History to Suicide Method and Gun Ownership for Men in San Diego**

| Group and Psychiatric History of Men Who Committed Suicide | Suicide Method: Shooting | Suicide Method: Other Than Shooting | Suicide Method: Leaping | Suicide Method: Other Than Leaping | Gun Ownership: Known to Own Gun | Gun Ownership: Known Not to Own Gun | Gun Ownership: Unknown |
|---|---|---|---|---|---|---|---|
| Consecutive suicides (N=143) | | | | | | | |
| Hospitalized | $16^{a}$ | $23^{a}$ | $5^{b}$ | $34^{b}$ | $13^{c}$ | $14^{c}$ | 12 |
| No known treatment | $43^{a}$ | $21^{a}$ | $0^{b}$ | $64^{b}$ | $39^{c}$ | $13^{c}$ | 12 |
| Outpatient | 10 | 5 | 1 | 14 | 10 | 3 | 2 |
| Unknown | 19 | 9 | 1 | 24 | 8 | 0 | 17 |
| Men under age $30^{d}$ | | | | | | | |
| Hospitalized | $10^{e}$ | $18^{e}$ | $5^{f}$ | $23^{f}$ | 10 | 10 | 8 |
| No known treatment | $27^{e}$ | $13^{e}$ | $0^{f}$ | $40^{f}$ | 22 | 12 | 6 |
| Outpatient | 8 | 7 | 1 | 14 | 8 | 4 | 3 |
| Unknown | 6 | 10 | 1 | 15 | 0 | 2 | 14 |
| Men age 30 and older (N=103) | | | | | | | |
| Hospitalized | 14 | 15 | $4^{g}$ | $25^{g}$ | $11^{h}$ | $12^{h}$ | 6 |
| No known treatment | 30 | 16 | $0^{g}$ | $46^{g}$ | $30^{h}$ | $8^{h}$ | 8 |
| Outpatient | 8 | 5 | 1 | 12 | 8 | 3 | 2 |
| Unknown | 11 | 4 | 0 | 15 | 8 | 0 | 7 |

[a] Significant difference between groups that used shooting and methods other than shooting (p=0.008; all comparisons used Fisher's exact test, one-tailed).

[b] Significant difference between groups that used leaping and methods other than leaping (p=0.007).

[c] Significant difference between groups that were known to own a gun and those known not to own a gun (p=0.02).

[d] N=99 for suicide method and 133 for gun ownership.

[e] Significant difference between groups that used shooting and methods other than shooting (p=0.009).

[f] Significant difference between groups that used leaping and methods other than leaping (p=0.009).

[g] Significant difference between groups that used leaping and methods other than leaping (p=0.02).

[h] Significant difference between groups that were known to own a gun and those known not to own a gun (p=0.01).

more immediately fatal methods. Only 2% of the women used guns for suicide during each time period.

Among the women in the San Diego study, only 17 (28%) of the 61 in the consecutive series, 13 (38%) of the 34 in the under-age 30 series, and 11 (23%) of the 47 in the age 30-and-older series had used a gun. There were no significant differences among these three groups in the proportion of women who had been hospitalized for psychiatric disorders compared to the proportion who had never received psychiatric treatment.

Of the men in the consecutive series and under-age 30 series who had used guns to commit suicide, a significantly smaller proportion had been hospitalized for psychiatric disorders than had never received psychiatric treatment (table 3). Among the men in all three series who committed suicide by leaping, significantly more had been previously hospitalized than had never received psychiatric treatment. Of the men in the consecutive series and age 30-and-older series who were known to have owned a gun, significantly fewer had been hospitalized for psychiatric disorders (table 3) than had never received psychiatric treatment.

## DISCUSSION

Two major competing hypotheses regarding the underlying cause of suicide have developed in the past century (6). Neither the sociological nor the psychiatric position has made it easy to approach the problem of suicide prevention.

Modifications of the availability and/or lethality of methods for committing suicide have been proposed as more immediate approaches to the problem of prevention. Major examples have been reported from other countries (7–14). A debate exists, however, as to whether any lasting changes in suicide rates resulted (15, 16). It has been argued that such maneuvers may lead to temporary decreases, but people who are determinedly suicidal eventually find some other way to commit suicide (17). Different ways of looking at epidemiological data related to these examples have resulted in continuation of this debate (18, 19).

The debate in the United States has focused largely on guns. A large number of suicides, particularly by men, are the result of gunshot wounds (20). The frequency with which both men and women, particularly in the younger age groups, use guns to commit suicide appears to have increased in the past several decades (21, 22). A concurrent increase in the production and availability of guns in the United States has occurred (23). Regional studies have suggested that higher suicide rates correlate with higher gun prevalence (24, 25) and lower rates correlate with stricter gun control statutes (26). Predictable criticisms of the interpretations of these data have appeared (23, 27, 28). Also, other speculations about the basis for increases in recent decades have been offered (29).

The question remains, however, as to whether significantly curbing the availability of guns across the United States would have a major effect on overall suicide rates. We believe the data from both Toronto and San Diego support the hypothesis that substitution of method would occur (1, 17). Several general limitations in our data must be recognized, however.

The feasibility of data collection must always be weighed against the desire for larger sample sizes and longer time spans. Our choice of 5-year periods for comparison of the Canadian data was based on practicality. Whether expansion of the years studied would provide different results and conclusions remains to be seen.

The strength of the Canadian data lies in the relative discreteness of the change. The Canadian law was activated across the board in 1978. Unlike the Massachusetts experience (30), an effort was made to collect existing guns in Ontario. While this effort was admittedly passive (i.e., authorities did not make searches of individual property), we were told by Ontario police authorities that thousands of guns were turned in and destroyed. Regardless of the lack of verification of this estimate, the statistically significant shift in suicide methods leads us to conclude that the law indeed had an effect.

Control populations are crucial in determining the real effectiveness of any specific change in conditions. Unfortunately from that standpoint, the Canadian law applied to all citizens. On the other hand, the relevant California statutes, which were all activated at least 10 years before this study, targeted only a limited population of psychiatric patients (3). We have no way of knowing whether those patients who had been hospitalized before committing suicide were actually reported according to California law or whether they even really had less access to guns. We did find that the previously hospitalized patients for whom we had the information were reported to have had significantly less access to guns in their homes than those who had never had psychiatric treatment (table 3). Regardless of whether the law was responsible for that or not, the difference was in the same direction as with the Canadian data. This consistency seems to further support the substitution hypothesis.

Missing data must also be considered. This is particularly bothersome in the San Diego study regarding history of prior psychiatric treatment. It is possible, for example, that all the male subjects with no information regarding treatment had, in fact, been hospitalized for psychiatric treatment. When we added those to the subjects known to have been hospitalized and repeated the Fisher tests, however, the probabilities were still significant ($p=0.04$ for the consecutive subjects and $p=0.004$ for the under-age 30 subjects). If we had assumed that they had not been hospitalized, the significances would have been magnified. Again, this manipulation appears to support the substitution hypothesis.

The proportion of suicides by gunshot among men in Toronto (table 2) was considerably lower than the U.S. rate (over 50%) even before 1978 (25). This probably reflects a historical difference in the attitude about gun ownership between the two countries above and beyond the legalities. Regardless of the explanation, the difference between countries makes it somewhat more difficult to use the Toronto data to predict the potential effects of such legislation in the United States. Again, however, the California data suggest that at least limited comparability of the effects of gun control on suicide may exist between the two countries.

The comparable shifts in proportion of suicides between gunshot and leaping for men in Toronto fit almost too closely. The California data support that shift as more than coincidental, however. Besides, in Toronto as well as in San Diego, there was no significant difference in the mean proportion of suicides due to "immediately fatal" methods (tables 2 and 3). Our concept of immediacy (31) is somewhat different from the definition of "violent" suicide (32). For the data presented here, however, the definitions are mutually inclusive. The apparent shift of methods in both locations appears to have been to another "more immediately fatal" method. This is consistent with Morris et al.'s observation in Philadelphia that, over a 75-year span, "men have consistently used violent and instantaneous means of suicide" (33). The actual method substituted, then, could be related more to the sex of the victim than to the availability of a particular method (34). Unfortunately (or fortunately, as the case may be), the numbers of women in both locations who used immediately lethal methods were small. No significant shift from guns to other methods was found. The possibility that the proposed substitution effect is not sex related, however, cannot be eliminated.

The possibility also exists that there may have been a pattern of change in annual suicide rate in Canada that was affected by the gun control law. We used a time series regression model to examine changes in rate over the two 5-year periods. We found that there was, indeed, an apparent slight upward slope (i.e., increase in rate) in the 5 years before the law and no slope (i.e., no change in rate) for the 5 years afterward. The difference in these slopes was not significant, however ($t=1.51$, $df>2\times10^7$, $p=0.13$). When the 1977 data point was excluded from consideration, however, there was no slope at all to that year, either. This would appear to add further strength to a conclusion that the gun control law did not affect the overall suicide rate in Toronto.

It is also reasonable to ask whether looking at overall rate changes might hide significant effects in other subpopulations. For example, we did find some possibly age-related differences in the suicides among men in San Diego. A significantly smaller proportion of the men in the younger series who used guns, compared to other methods, had been hospitalized (table 3). This was not true of men in the older series. If one accepts the possibility of a relationship between this finding and the California law, one might conclude that the older subjects had guns left over from before enactment of the law. This conclusion was not supported, however, by the finding that significantly fewer older men who were known to own a gun were also known to have been hospitalized (table 3). Both of these sets of data are limited by missing information, and any conclusions have to be qualified by that. Nonetheless, in spite of the differences in significance, the findings for both age groups are consistently in the direction of an effect of hospitalization. Interestingly, this was true for the women as well. Again, the possibility of an age-related effect of the proposed substitution hypothesis cannot be discounted.

We believe the data reported here suggest conservative expectations regarding the potential effects of widespread gun control on overall suicide rates. It goes without saying, however, that studies of this question should continue. Well-controlled prospective investigations seem impossible. Consequently, only data from a variety of "natural experiments" in different settings will eventually answer this tantalizing question. Until then, clinicians should certainly continue to advise families and friends of suicidal persons in order to limit their access to guns. Removal of guns, however, should not lull anyone into a false sense of security regarding the potential for a suicidal person to substitute an equally immediately lethal method. It seems unlikely that all potential suicide methods could ever be removed, even in psychiatric hospitals (35). We agree with Whitlock (19) that the more potentially productive approach to the problem will be to find better methods for identifying truly suicidal persons and effectively treating their underlying psychiatric illnesses.

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# Patterns of Sex Differences in Negative Symptoms and Social Functioning Consistent With Separate Dimensions of Schizophrenic Psychopathology

Robert H. Dworkin, Ph.D.

*In 220 schizophrenic twins, men had greater asociality-withdrawal and poorer premorbid social competence than women but there were no sex differences in symptoms, suggesting that negative symptoms and social functioning reflect different processes in the development and manifestation of schizophrenia and that they should be examined separately.*

(Am J Psychiatry 1990; 147:347–349)

Negative symptoms have received increasing attention in recent research on schizophrenia. In these studies, affective deficits and certain types of thought disorder (e.g., poverty of speech) are typically considered negative symptoms, which are distinguished from positive symptoms such as delusions and hallucinations. The role of social functioning in the negative symptom syndrome, however, has not been consistently specified. Although Andreasen (unpublished 1984 manual) considered asociality a negative symptom and included it in her influential Scale for the Assessment of Negative Symptoms (1), Strauss et al. (2) proposed that disordered social relationships reflect an independent process in the development of schizophrenia, and Crow (3) argued that social withdrawal is complex and might sometimes be a consequence of positive symptoms. There is evidence that premorbid social competence and negative symptoms are associated (1), but it is not possible to determine from available data whether disordered social functioning is, as Andreasen suggested, one type of negative symptom, or whether it reflects a separate process in the development of schizophrenia.

In previous research (4), my associates and I examined the relationship of negative symptoms, positive symptoms, and social competence to concordance for schizophrenia in monozygotic twins; we presented evidence suggesting that these three types of symptoms reflect relatively independent processes. In the present study, patterns of sex differences in negative symptoms and social functioning are reported that provide further evidence that negative symptoms and social functioning are separate processes in the development and manifestation of schizophrenia.

## METHOD

The case histories of monozygotic schizophrenic probands and their co-twins from the five twin studies of schizophrenia with case histories published in English were assembled. These 302 case histories were intermixed randomly and carefully edited to remove all information regarding zygosity as well as any material that might enable a rater to match a proband with his or her co-twin. The following analyses of sex differences are based on the 151 schizophrenic proband twins examined previously (4), combined with the 69 co-twins who were considered schizophrenic by the original investigators. Of these twins, 108 were women and 112 were men; all had been carefully diagnosed according to traditional European criteria for

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**TABLE 1. Sex Differences in Symptoms and Social Functioning in Schizophrenic Twins**

| Measure | Intraclass Correlation Reliability Between Raters (N=220) | | Women (N=108) | | Men (N=112) | | Z[b] | p[c] |
|---|---|---|---|---|---|---|---|---|
| | Individual Ratings | Mean Ratings[a] | Mean | SD | Mean | SD | | |
| Positive symptoms | 0.82 | 0.90 | 3.19 | 1.33 | 3.12 | 1.40 | 0.30 | 0.76 |
| Venables-O'Connor Scale for Rating Paranoid Schizophrenia | 0.77 | 0.87 | 7.71 | 3.16 | 7.22 | 3.07 | 1.18 | 0.24 |
| Negative symptoms | 0.70 | 0.82 | 2.22 | 1.35 | 2.50 | 1.16 | 1.50 | 0.13 |
| Negative-4 symptoms (excluding asociality-withdrawal) | 0.68 | 0.81 | 1.63 | 1.12 | 1.75 | 0.97 | 0.87 | 0.38 |
| Asociality-withdrawal | 0.48 | 0.64 | 0.59 | 0.42 | 0.75 | 0.37 | 3.02 | 0.003 |
| Phillips Abbreviated Scale of Premorbid Sexual Adjustment[d] | 0.90 | 0.95 | 2.96 | 2.15 | 4.05 | 2.11 | 3.48 | 0.0005 |
| Zigler-Phillips Social Competence Scale[e] | 0.69 | 0.82 | 0.92 | 0.37 | 0.79 | 0.36 | 2.56 | 0.01 |
| Age at onset (years) | — | — | 32.10 | 10.46 | 28.00 | 6.86 | 2.66 | 0.008 |

[a] Equivalent to Cronbach's alpha.

[b] N=220 except for the Phillips scale (N=200), Zigler-Phillips scale (N=212), and age at onset (N=206); data missing for some variables in some of the case histories.

[c] Conventional significance levels based on two-tailed Mann-Whitney U tests. The significance level based on multistage Bonferroni procedure was $p \leq 0.05$ for asociality-withdrawal, Phillips scale, Zigler-Phillips scale, and age at onset.

[d] Higher scores reflect poorer premorbid competence.

[e] Lower scores reflect poorer premorbid competence.

schizophrenia, and most had received a hospital diagnosis of schizophrenia.

For each of these schizophrenic twins, five negative symptoms (affective flattening, alogia, avolition-apathy, asociality-withdrawal, and attentional impairment) and five positive symptoms (delusions, hallucinations, bizarre behavior, positive formal thought disorder, and catatonic motor phenomena) were rated by a clinical psychologist and a psychiatrist. The raters used a manual (5) that included definitions of positive symptoms drawn from the literature of descriptive psychiatry and a modification of Andreasen's interview-based Scale for the Assessment of Negative Symptoms (1; unpublished 1984 manual), which we adapted for use with case histories. Each individual received two scores, one for negative symptoms and one for positive symptoms, that could range from 0 to 5. Because asociality-withdrawal, a measure of poor social functioning after the onset of schizophrenia, was included in the negative symptoms scale, ratings of asociality-withdrawal and a measure of negative symptoms that excluded this symptom, negative-4, were also analyzed separately.

A second clinical psychologist and an advanced clinical psychology graduate student rated each of the twins on the Phillips Abbreviated Scale of Premorbid Sexual Adjustment (6) and on the Zigler-Phillips Social Competence Scale (7) for level of social functioning before the first documented psychiatric hospitalization.

The Venables-O'Connor Scale for Rating Paranoid Schizophrenia (8)—an additional measure of one type of positive symptom (paranoia)—was subsequently rated by the advanced clinical psychology graduate student who approximately 1 year earlier had rated the two measures of premorbid social competence. The second rater for the proband twins was the clinical psychologist who 3 years earlier had rated positive and negative symptoms, and the second rater for the cotwins was the clinical psychologist who 2 years earlier had rated the two measures of premorbid social competence. Age at onset of schizophrenia was also coded.

## RESULTS

The interrater reliabilities of the ratings, presented in table 1, were generally excellent, and the means of the two raters have been used in the following analyses. Two-tailed Mann-Whitney U tests were used to test the significance of the differences between the male and female schizophrenic twins, and a multistage Bonferroni procedure was used to control for multiple tests of significance. As can be seen in table 1, male and female schizophrenic twins did not differ significantly in positive symptoms, paranoid symptoms, negative symptoms, or negative-4 symptoms. There were, however, significant sex differences in asociality-withdrawal, both measures of premorbid social competence, and age at onset.

## DISCUSSION

In our data, men with schizophrenia had significantly greater asociality-withdrawal after the onset of their illness, poorer premorbid social competence, and younger ages at onset than women. There were no sex differences, however, in either measure of negative symptoms or in either measure of positive symptoms. Although these analyses of sex differences were based on case histories of twins that were prepared before recent attention to the distinction between positive and negative symptoms, the data are consistent with research on social competence and positive and negative symptoms in nontwin patients with schizophrenia (9; unpublished 1985 paper of R.J. Lewine and A.A. Sommers). It is beyond the scope of this paper, however, to attempt to account for these patterns of sex differences.

Inasmuch as there were sex differences in asociality-withdrawal and premorbid social competence but not in symptoms, the results provide support for the suggestion of Strauss et al. (2) that negative symptoms and disordered social relationships reflect separate functional processes in the development of schizophrenia. Complementing these analyses of sex differences, the results of twin concordance analyses (4, 5) and confirmatory factor analyses of the correlations among positive and negative symptoms and social functioning (10; unpublished paper of M.F. Lenzenweger et al.) have also provided support for the relative independence of these dimensions of schizophrenic psychopathology.

The results of this study suggest that social functioning should be examined separately from negative symptoms in future research on schizophrenia, not simply included as one component of a negative symptoms scale. A further implication of the results is the additional support they provide for a multidimensional approach to schizophrenia (2–5, 10), an approach that emphasizes the study of relatively independent dimensions of symptoms and their underlying processes.

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# Relationship of Cognitive Factors to CSF Corticotropin-Releasing Hormone in Depression

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*The authors investigated the relationship between items on the Beck Depression Inventory and CSF levels of corticotropin-releasing hormone (CRH) in 17 depressed patients. Linear regression analysis showed that self-accusation, expectation of punishment, and crying accounted for 82% of CRH variance.*

(Am J Psychiatry 1990; 147:350–352)

Dysregulation of the hypothalamic-pituitary-adrenal (HPA) axis is found in 40%–60% of depressed patients. Although the regulation of the HPA axis is complex, recent infusion and CSF studies of corticotropin-releasing hormone (CRH) have suggested that hypersecretion of CRH from the paraventricular nucleus in the hypothalamus may play a role in the dysregulation of the HPA axis found in depression (1–4).

Cognitive theories hypothesize that the origin of depression lies in cognitive schemata, which include negative beliefs about oneself, the world, and the future (5, 6). Such trait variables may partly determine state-dependent cognition found in depression (5–7).

In order to test the hypothesis that CRH levels may be related to cognition, scores on cognitive items from the Beck Depression Inventory were analyzed to ascertain their relationship to CSF levels of CRH.

## METHOD

We studied a consecutive series of 17 depressed inpatients at the National Institute of Mental Health. Fourteen patients met the *DSM-III* criteria for major depressive episode with melancholia, and three met the criteria for major depressive episode without melancholia. Each patient completed the Beck Depression Inventory (5).

Before undergoing lumbar puncture, the patients were placed on a low-monoamine, alcohol-free, and caffeine-restricted diet. Patients who were taking psychotropic medications were slowly withdrawn from them and were medication free for at least 2½ weeks before lumbar puncture. Lumbar puncture was performed between 8:30 and 9:00 a.m. with the subject in the lateral decubitus position. Each subject had fasted and had been at bed rest since the midnight before the lumbar puncture. The first 10 ml of CSF were collected as a pool and placed on ice at the bedside; the sample was subsequently divided into equal parts and frozen at −80 °C until assay. CSF levels of CRH were assayed by means of a previously described radioimmunoassay (3).

The analysis included all seven specifically cognitive items on the Beck inventory: pessimism, sense of failure, guilt, expectation of punishment, self-dislike, self-accusation, and suicidal wishes. Additional factors with a potential for confounding effects—age and affect (represented by the Beck sadness and crying items)—were also examined. Pearson correlation coefficients were calculated to evaluate the relationship between CSF levels of CRH and scores on individual items. We also performed three linear regression analyses to try to predict CSF levels of CRH: the first used individual cognitive items, the second used the two affect items, and the final analysis involved a combination of the two sets of predictors.

## RESULTS

The 17 depressed patients consisted of 15 women and two men whose mean±SD age was 40.8±10.3 years. The mean±SD duration of depression was 7.4 ±6.7 months; the range was 3 weeks to 2 years. The mean±SD Beck inventory score was 36.0±10.9.

Correlations between CSF levels of CRH and total scores on the Beck inventory were not significant ($r=-0.31$, $N=17$, $p<0.23$). Correlations between CSF levels of CRH and total scores on the cognitive items were also not significant ($r=-0.38$, $N=17$, $p<0.13$). However, both self-accusation and crying were strongly and negatively related to CSF levels of CRH, although they appeared to be relatively independent of each other (see table 1). Sadness was correlated with

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**TABLE 1. Intercorrelations of Beck Depression Inventory Items and CSF Levels of Corticotropin-Releasing Hormone in 17 Depressed Patients**

| Variable | Pessimism | Sense of Failure | Guilt | Expectation of Punishment | Self-Dislike | Self-Accusation | Suicidal Wishes | Sadness | Crying |
|---|---|---|---|---|---|---|---|---|---|
| Cognitive items | | | | | | | | | |
| Pessimism | | | | | | | | | |
| Sense of failure | 0.50[a] | | | | | | | | |
| Guilt | 0.52[a] | 0.79[b] | | | | | | | |
| Expectation of punishment | 0.36 | 0.65[c] | 0.81[b] | | | | | | |
| Self-dislike | 0.42 | 0.68[c] | 0.78[b] | 0.74[b] | | | | | |
| Self-accusation | 0.25 | 0.54[a] | 0.53[a] | 0.51[a] | 0.79[b] | | | | |
| Suicidal wishes | 0.52[a] | 0.17 | 0.26 | 0.34 | 0.49[a] | 0.56[a] | | | |
| Affect items | | | | | | | | | |
| Sadness | 0.56[a] | 0.28 | 0.45 | 0.46 | 0.29 | 0.07 | 0.51[a] | | |
| Crying | −0.08 | 0.02 | 0.16 | 0.04 | 0.21 | 0.38 | 0.17 | 0.20 | |
| CSF level of CRH[d] | −0.10 | −0.27 | −0.23 | −0.05 | −0.40 | −0.72[b] | −0.43 | −0.02 | −0.75[b] |

[a] $p<0.05$.
[b] $p<0.001$.
[c] $p<0.01$.
[d] Division of 0.05 (two-tailed) probability by nine correlations, using the Bonferroni correction, indicates that a p value <0.006 is significant.

pessimism and suicidal wishes—both cognitive items reflecting negative attitudes toward the future—but was clearly unrelated to CSF levels of CRH. Age was not related to CSF levels of CRH or to any of the individual item scores. There were significant intercorrelations between individual Beck inventory cognitive items (table 1).

The initial linear regression analysis used all cognitive items to predict CSF levels of CRH. Self-accusation, entered first, was associated with a sizable decrease in CSF levels of CRH (adjusted $R^2=0.48$, $F=16.02$, $df=1, 15$, $p<0.0013$). When the effect of self-accusation was removed, a suppressed cognitive variable, expectation of punishment, was found to have a significant effect, directionally opposite to that of self-accusation (adjusted $R^2=0.60$, $F=13.15$, $df=2, 14$, $p<0.0007$; standardized regression coefficient $[\beta]=-0.94$ for self-accusation and 0.42 for expectation of punishment).

A second linear regression was performed entering the items sadness and crying. Only the second of these was a significant predictor of CSF levels of CRH. This item accounted for over one-half the variance in CSF levels of CRH (adjusted $R^2=0.54$, $F=19.45$, $df=1, 15$, $p<0.0006$; $\beta=-0.75$).

A final regression analysis entered the item crying after cognitive predictors had been removed. Addition of this indicator achieved a significant increase in prediction (adjusted $R^2=0.82$, $F=25.75$, $df=3, 13$, $p<0.0001$; $\beta=-0.69$ for self-accusation, $\beta=0.32$ for expectation of punishment, and $\beta=-0.50$ for crying).

## DISCUSSION

Our previous study (3) found no significant difference between depressed patients and control subjects in CSF levels of CRH. Regression analysis in the present study, however, indicated that two of the Beck inventory cognitive items were strongly predictive of CSF levels of CRH in the depressed patients. There was no significant relationship between CSF CRH and the total cognitive item score, sadness, or the total Beck depression score. Thus, the results of the study suggest the intriguing possibility that specific cognitive factors in depressed patients may be related to CSF levels of CRH.

The main cognitive concomitant found in the study, self-accusation, may be akin to the psychodynamic concept of hostility turned inward, which has been postulated in certain types of depression (8). This cognitive element was associated with low CSF levels of CRH. Expectation of punishment was found to act as a classical suppressor in this relationship, accounting for a significant amount of variance by apparently moderating the relationship. The role of the independent predictor crying is also intriguing.

The results of this study suggest the possibility of an interaction between the cognitive phenomena and the pathophysiology of depression. However, the interpretation of these preliminary data can only be speculative. The findings may be state dependent, since the study was cross-sectional; patients were studied only when they were depressed. Future prospective studies should be longitudinal. They should examine relationships between biological variables and the specific cognitive variables identified in this study, studying patients both when they are depressed and when they have recovered.

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# Book Forum

## Nancy C. Andreasen, M.D., Ph.D., Editor

## AFFECTIVE DISORDERS

**Lithium Treatment of Manic-Depressive Illness: A Practical Guide, 4th ed.,** *by Mogens Schou. Basel, Karger, 1989, 46 pp., $10.00 (paper).*

This booklet is written by the foremost authority on the pharmacology of lithium. Its main purpose is to help patients who receive lithium and their relatives and caretakers to understand the benefits and risks of this treatment. To make this understanding deeper and more relevant, there is a good description of the psychopathology and natural history of manic-depressive illness. The book is also directed to the average psychiatrist and other physicians, who would benefit from a quick glance at the information in the booklet. It answers several questions relating to lithium therapy.

Clearly written and mostly jargon free, the book simplifies relatively complex concepts of lithium treatment and manic-depressive illness, and a very useful glossary is included to help patients and their relatives understand the meaning of some of the technical terms used. The sections progress logically from a description of the manifestation of manic-depressive illness and its treatment before the introduction of lithium, to the use of lithium for treatment of mania specifically and for prevention of affective illness in general, to the practical aspects of lithium therapy, to side effects and risks and "do's and don'ts" of lithium treatment.

This book is recommended for patients who receive lithium therapy, their relatives, and their physicians and nurses. Because it is relatively inexpensive, this book should be abundantly available for distribution to patients and relatives in clinics and hospitals. Dr. Schou should be praised for this very useful and informative booklet; it can be of great help to those who suffer from or deal with manic-depressive illness.

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**Depressive Illness: Prediction of Course and Outcome,** *edited by T. Helgason and R.J. Daly. New York, Springer-Verlag New York, 1988, 146 pp., $55.90.*

I have every reason to believe that I might never have come across this book had I not been asked to prepare a review of it, short of carrying out a methodological search into the literature on depression. Even then, it is always difficult to separate the wheat from the chaff. And that would have been most unfortunate, for this small volume is one of the crispest, most salient, and most coherent reviews of any topic in psychiatry that I have read.

The various chapters cover the entire range of issues having to do with the nature of affective illness or, as P. Pichot in his discussion rightly prefers, mood disorders. The chapters attend to the clinical course of such disorders; genetic contributions; psychosocial factors influencing both course and outcome; biological factors, including due attention to metabolic processes and such modern assessment techniques as positron emission tomography and computerized EEG; the observed relationships among mood disorders, death rates, and physical illness; and personality traits that may predispose to illness and make recovery and life adaptation more difficult afterward.

Its organization and style make this book remarkable. It is a truly edited presentation—clear, precise, with practically no repetitiveness, a pleasure to read, and a model of communication. Consider J. Angst's first chapter, "Clinical Course of Affective Disorders." Each section of this chapter ends with a conclusion that can be read before going back and reading the section itself. Angst's discussions are precise and extensively documented. The reader can draw meaningful conclusions about what is and is not currently known about mood disorders. For example, bipolar conditions are probably more frequent than has been appreciated. Manic episodes are more common in men. Tricyclic antidepressants induce cycling. Seasonal factors have been overestimated. The average duration of a depressive episode is 6 months, compared with 4 months for a manic episode. About 10% to 20% of patients become chronically disabled. The mortality rate, due partly to suicide, is higher and the risk of various physical diseases such as cardiovascular illness is greater in patients with mood disorders than in control groups. Retrospective studies seriously lack the informativeness and reliability of prospective ones.

Throughout the book the same clarity persists. E. Smeradli concludes that "in genetic studies of psychiatric disorders we work with the segregation of disease susceptibility, *not* with the segregation of the disorder itself." V. Lehtinen emphasizes the need for a new definition of the concept of depression, and H.S. Akiskal describes the cyclothymic, hyperthymic, and dysthymic personality structures as preceding a major disorder of mood and seriously complicating the process of recovery and rehabilitation.

In the search for more hypotheses with which to examine the nature of depression, I would naturally have been pleased had reference been made to some of my own writings in which I have positioned the experience of depression within the framework of a natural cycle of disruption and reintegration throughout life in response to stressful events and changes. From this vantage point, the mood changes themselves are not seen as illness but, rather, the inability to enter into them, manage to keep them within certain limits, and, ultimately, recover from them with a more complex, adaptive personality structure. I believe that this "resilience hypothesis" reduces the stigma still loudly associated with disability, particularly disability of psychiatric origin, and that it also motivates patients, families, and physicians to seek and comply with intelligent treatment regimens. This would attack the reason for J.R.M. Copeland's observation in this book that only 4% of a community sample of depressed subjects in Liverpool received treatment from their general practitioners specifically for depression. The resilience hypothesis can also help reframe some of the findings from psychosocial and biological research, not unlike the suggestions given here by H. Katschnig and D.O. Nutzinger, who describe the "vulnerability-external influence" and "interactive developmental" models of mood disorders.

This volume represents the proceedings of a workshop held in 1985 sponsored by the Study Group on Mental Illness Research of the European Medical Research Council. The publishers suggest that it will be a valuable reference for young researchers and perhaps older ones as well. Their comments do a disservice. In spite of the fact that the material is already more than 3 years old (psychiatry does not have the reputation for being a field exploding with discoveries), I believe that the book presents a very useful and pertinent opportunity for clinicians not directly engaged in research to quickly review the highlights of modern thinking about the nature and origins of mood disorders.

Certainly this book contains a lesson for us all. A book's value is not measured by its length or by its unreadability but by good writing further honed by careful editing and, above all, clear, substantial thinking on the part of the authors.

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**New Concepts in Depression: Pierre Fabre Monograph Series, vol. 2,** *edited by M. Briley and G. Fillion. Houndmills, Great Britain, Macmillan (Dobbs Ferry, N.Y., Sheridan House, distributor), 1988, 362 pp., $95.00.*

In March of 1987 an international symposium was held to review the most recent research information and hypotheses concerning neuropharmacological aspects of affective disorders. This volume is a multiauthored monograph from that symposium. As might be expected of such a conference, the book is highly technical, offers new data as well as reviews of old data, advances new hypotheses regarding affective illness, and reviews those which have been previously offered. At least half of the book is devoted to the role of serotonin in affective disorder. An additional quarter is devoted to neuroendocrine perturbations in affective disorder, and the remaining quarter covers a miscellaneous group of subjects such as thermal response of membrane activity, the role of the $\gamma$-aminobutyric acid (GABA) receptor in affective illness, and the role of nutritional status and carbohydrates in brain function and mood regulation.

For researchers and students of affective disorder, this volume is must reading. Some of the most interesting findings include the following.

1. Serotonin (5-HT) levels are increased by monoamine oxidase inhibitors (MAOIs); this is followed by reduced 5-HT presynaptic release. When 5-HT levels are increased by a 5-HT reuptake inhibitor, however, 5-HT release remains unaltered. This suggests that the function of presynaptic 5-HT autoreceptors is modulated by 5-HT uptake blockers.

2. Substance P and thyrotropin-releasing hormone (TRH) are localized in some 5-HT nerve terminals. In the spinal cord, substance P reduces binding affinity of 5-HT$_1$ receptor sites. TRH and 5-HT interact, and TRH may play a role in the long-term adaptation of 5-HT receptor function produced by antidepressants. TRH may also act directly on postsynaptic 5-HT$_2$ receptors to regulate binding and responses caused by these receptors. Chronic imipramine treatment reduces 5-HT utilization and increases substance P immunoreactivity but does not affect TRH immunoreactivity. This suggests that some 5-HT comodulaters may play a role in the therapeutic activity of antidepressant drugs.

3. There is a high-affinity 5-HT receptor site related to stimulation of adenylate cyclase that has been pharmacologically characterized as 5-HT$_{1D}$. It is a postsynaptic 5-HT receptor that may play a role in the pathology of depression and may also play a role in the modulatory activity of 5-HT in other neurotransmitter functions.

4. The 5-HT autoreceptor may be of the 5-HT$_{1B}$ subtype.

5. The hypothesis is put forth that anxiety, aggression, and mood are each regulated by 5-HT but that different 5-HT projections may be involved. In this manner, 5-HT resembles dopamine-related projection systems. Available tryptophan may be reduced by circulating corticosteroids, which reduce the enzyme tryptophan pyrolase and therefore decrease the amount of tryptophan available for 5-HT synthesis. Plasma folate levels are also decreased in depression, and 5-HT levels are related to tetrahydrobiopterin, which is a cofactor for hydroxylation of tryptophan.

6. There is a reduction in the number of platelet imipramine bindings sites in elderly patients with major depressive disorder but not in elderly patients with Alzheimer's disease. Platelet imipramine binding, therefore, may be a useful diagnostic tool to discriminate between these two states.

7. The efficacy of lithium enhancement of response to antidepressant response is greatest with MAOIs and with tetracyclic drugs. This enhancement is superior to lithium's enhancement of the antidepressant effect of ordinary tricyclics or 5-HT reuptake blockers. Low plasma levels of lithium are sufficient to potentiate antidepressant drug effects.

8. Down-regulation of $\beta$-noradrenergic receptors may not be specific to the antidepressant effect of these drugs: a number of therapeutic antidepressant drugs do not down-regulate the receptors. Similarly, data from peripheral autonomic systems argue against down-regulation of presynaptic $\alpha_2$ receptors as the reason for the therapeutic effect of chronic antidepressant treatment.

9. The accumulation of homovanillic acid in the CSF is lower in depressed patients, especially in those with marked psychomotor retardation. This finding argues for a role for dopamine in depression or at least in agitation.

10. Opiate peptides induce a presynaptic inhibition of the release of most hypothalamic neuropeptides.

11. Second messenger transduction systems can affect one another. Cyclic AMP, for example, can inhibit phospholipase-C. Conversely, secondary products of phospholipase-C activation, such as prostaglandins, can directly stimulate adenylate cyclase.

12. Cerebral opioid peptides may play a role in mood regulation and may be involved in the pathophysiology of affective disorders as well as in the action of antimanic and antidepressant treatments.

13. Evidence is accumulating that points to an interaction between $\alpha$-adrenergic and $\beta$-adrenergic neurotransmitter systems. $\alpha_2$-adrenergic agonists amplify the response to the $\beta$-adrenergic agonist isoproterenol.

14. Responses of clonidine and apomorphine challenges to growth hormone (GH) release may suggest differential neurotransmitter dysfunction in affective illness. A normal GH response to clonidine may suggest a serotonergic-type depression and response to a serotonergic-type drug. A blunted GH response to clonidine would correspond to a central noradrenergic hyposensitivity and suggest the need for a drug that increases noradrenergic neurotransmission. A blunted GH response to apomorphine could correspond to a

lower sensitivity in central dopaminergic receptors and, therefore, is consistent with a better treatment outcome following the administration of antidepressants that increase dopaminergic neurotransmission.

15. A hypothesis is put forth suggesting that depression is due to an imbalance in second messengers: depression results from reduced function of the cAMP pathway and mania results from the converse. This hypothesis also explains the therapeutic and prophylactic effect of lithium in bipolar depression. In mania, lithium dampens the overactive adenylate cyclase system. In depression it prevents the overactivity of the phospholipase-C system.

16. If there is a reduction in cAMP activity in depression, then increase in cAMP through the use of a phosphodiesterase-C inhibitor should have a therapeutic effect. Evidence is presented to suggest that rolipram, a cAMP-selective phosphodiesterase inhibitor, has antidepressant activity.

17. There may be a decrease in GABA function in affective disorders characterized by a higher level of anxiety. There is an increase in diazepam binding inhibitor immunoreactivity in the CSF of depressed patients that might reflect impairment of central GABA function in depression.

As should be evident, this volume will offer great rewards to research-oriented psychiatrists and students of the neurobiology of affective disorders. Because of its extreme technical content and research orientation, however, it is not recommended for the practicing clinician.

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**Affective Disorders,** *edited by Frederic F. Flach. New York, W.W. Norton & Co., 1988, 238 pp., $29.95.*

I have the impression that in recent years the number of books on depressive illness has burgeoned. My initial reaction to this book, therefore, was, "Well, here is another book on depression." I wondered whether readers of the *Journal* had not already been inundated with reviews of such books. Looking through all the issues of 1988, however, I was surprised to count only eight reviews of books related to depression. I was also surprised to find that there were more than 45 reviews of books related to topics in psychoanalysis and psychodynamics. If these numbers are related proportionally to what psychiatrists and mental health workers read, then the perceived ascendancy of descriptive, biological, and data-oriented psychiatry may be no more than wishful thinking. Facts are few and theories abundant. Fortunately, this book is largely a factual presentation of the current state of knowledge about some aspects of depressive illness.

The editor introduces the book with some thoughtful remarks about the variety of emotions that present themselves under the guise of depression. He postulates that depressed patients have diminished "psychobiological resilience." Biological and psychological treatments of depressive patients result in enhanced resilience. The chapters following this introduction are contributions by well-known experts on the topics they present. All are well written but have some stylistic differences, which is conducive to pleasurable reading. Some of the topics relate to studies in the forefront of psychiatric research; others travel down the well-beaten track.

The first chapter, by R.C. Whybrow, concerns developmental aspects of the individual as a growing person who experiences attachments and separations. Whybrow postulates that the failure properly to integrate and resolve experiences of loss leads to vulnerability for depression. Regrettably, the vagueness of the terms "attachments" and "separations" makes it very difficult to understand or test the author's hypothesis. This chapter, although quite readable, is long on theory and short on data. Dealing with the same topic, Alec Roy in another chapter deftly reviews the role of loss or separation by referring to data from his own and others' research. These data show that early parental loss or separation may be a risk factor for some depressive reactions but the majority of depressive patients do not have parental losses in their early life.

Only the chapter by R. O'Connell touches on the diagnostic criteria for affective disorders, mostly in terms of unipolar versus bipolar illnesses. He presents a concise overview of the history, phenomenology, course, and treatment outcomes in these conditions. M.B. Keller et al. review more than a dozen studies of therapeutic response and outcome in depression, starting with Kraepelin and moving on to more recent studies, including their own work. They report rates of chronicity that vary from 4% to 22%. The meaning of these statistics is difficult to grasp, however, because of the changing diagnostic styles and therapeutic interventions over the years. All they tell us is that depression is diagnosed differently at different times and according to different people, that different treatments are applied, and that the people diagnosed by the various systems respond differently and have different courses.

In respect to treatment, the chapter by T.A. Ban and M.H. Ebert on treatment of depression in the elderly is most informative and provides practical guides for diagnosis and treatment in this population. A. Storr discusses the psychotherapy of patients with depressive personalities from a psychodynamic point of view. This chapter is largely theoretical and does not provide any data on the usefulness of psychodynamic psychotherapy. R.B. Jarret and A.J. Rush provide an incisive review of the principles of cognitive therapy in depression. They review data from comparative studies in which cognitive therapy alone, medications alone, or medications in combination with cognitive therapy were administered. They show that the efficacy of cognitive therapy was as good as medication in treating patients who had moderate degrees of depression but were not psychotic. Related to treatment with antidepressants, J.M. Davis et al. provide a thoughtful and critical review of the role of assessing plasma antidepressant levels. They suggest that the fashionable concept of a "therapeutic window" is not generally applicable and that the clinical status of the patient should be an important gauge for dosing. Plasma levels are most useful when they show low levels of the drugs.

S.M. Mirin and B. Woodward discuss the clinical aspects and pharmacotherapy of depression in alcoholics. They provide very useful suggestions for the diagnosis of depression in alcoholic patients and the variety of therapeutic modalities that can help them. B. Pflug provides an up-to-date review of techniques for the treatment of depressive patients by sleep deprivation. Sleep deprivation seems to be quite effective for unipolar-endogenous depression, but neurotic depression does not respond so well. F.M. Jacobson and N.E. Rosenthal present interesting data on the technique and usefulness of phototherapy in the treatment of patients with seasonal affective disorder.

There are also informative chapters of theoretical interest by E.M. Levy and R. Krueger on the immune system in depression and by T.H. Monk on circadian rhythms affecting human performance. I should not fail to mention that preceding each chapter the editor provides a few comments and summarizes the chapter. Whether these comments add to or detract from the interest of the reader is difficult to say. Personally, as I went through the book I found myself resisting these editorial notes.

On the whole, this book offers a variety of important data and knowledge about well-known and some not-so-well-known topics in depression. Most chapters are written in a very readable style, and all the important aspects of a topic are presented with economy and simplicity. This book would be useful mostly for physicians in an academic setting or advanced practice, but there are chapters that could be used by psychiatrists taking care of patients in diverse clinical situations. Such psychiatrists would benefit from the fund of knowledge available in this book.

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Treating Resistant Depression, *edited by Joseph Zohar, M.D., and Robert H. Belmaker, M.D. New York, PMA Publishing Corp., 1987, 411 pp., $50.00.*

The introduction of effective treatments for affective disorders necessarily defined a new group of patients, namely, those suffering from "treatment-resistant" depression. Over the years there has been no dearth of symposia, no dearth of literature, and indeed no dearth of suggestions regarding the appropriate diagnosis and treatment of treatment-resistant depression, but there has been and continues to be a striking dearth of data.

The very term "treatment resistant" and its synonyms, "treatment refractory" and "nonresponder," imply that certain prerequisites have been met. First, it would seem intuitively obvious that there has to be an appropriate match between the diagnosis and the treatment. Second, a standard for adequacy of treatment has to be met to distinguish patients who are inadequately treated from those who are truly treatment resistant. Third, consensus has to exist as to what number of proven treatments a patient must "fail" to respond to before being classified as treatment resistant. Unfortunately, most authors do not agree on a definition of "treatment resistant." Consequently, edited volumes such as this contain some chapters that are excellent and some that are so flawed by methodological problems as to be worthless if not misleading.

The introductory chapters of this book are helpful, especially the unusually clear paper by Links and Akiskal, which crisply addresses the issue that not all chronic depressions are treatment resistant and actually offers a good working definition of adequate treatment for depression. The chapter by Thase and Kupfer on the clinical characteristics of treatment-resistant depression is also solid but presents the first example of a problem that is prevalent throughout the book. That is, the summary tables are not accurate reflections of the text. Since clinicians often look to such tables to refresh their memory, this is not an insignificant problem. Specifically, in the table of clinical correlates of nonresponse, delusions and agitation are both listed as variables that predict nonresponse to tricyclic antidepressants. However, although there are overwhelming data that delusional depressions do not respond to tricyclic antidepressants, the data on agitation as a predictor of nonresponse are scanty and contradictory. This difference is clearly presented in the text, but the table is a misleading condensation of the chapter. The last of the introductory chapters, on the psychological management of resistant depression by Greenberg and Spiro, is a pleasant surprise because it does not represent the standard tiresome polemic on psychological versus biological perspectives. Rather, the authors offer practical approaches to psychological management that should be applied along with medication trials.

The next section of the book covers the adequate use of standard treatments for affective disorder. The first and probably the most critical chapter is by Gold et al., who discuss the use of blood levels to define adequate tricyclic treatment and, therefore, by implication, the tricyclic nonresponder. Unfortunately, the authors' relatively careful approach is sabotaged by the table, which indicates that there are meaningful plasma level measurements for drugs such as trazodone, amoxapine, or maprotiline. Once again, although the text is more careful than the table, the clinician, on the basis of a relatively meaningless laboratory value, will be misled into concluding that an "adequate" trial of a drug has been given.

Montgomery's chapter is an excellent, thoughtful review of whether the purported differences in mechanism of action between various antidepressant medications (e.g., preferential blockade of reuptake of norepinephrine versus serotonin) have relevance for clinical practice. He concludes that "pharmacological specificity does not have clinical relevance for response" and, further, after a careful review of the available literature, that if a patient does not respond to one tricyclic antidepressant "there is no sound pharmacological basis for making the change from one to another." The other chapters in this section are also generally good, particularly the review by de Montigny and Cournoyer of the effect of lithium as an augmentation treatment with tricyclics, although the chapter on monoamine oxidase inhibitors (MAOIs) by Shawcross and Tyrer is somewhat disappointing in that it does not sufficiently review the data on the effect of MAOIs in atypical depression.

The final section of the book is devoted to adjunctive measures—nonstandard treatments that are used after the standard treatments have failed. Unfortunately, a section such as this often includes a predominance of authors who are promoting a particular treatment rather than carefully considering the available data. The chapter by Pohl and Gershon on the use of new antidepressants in tricyclic-resistant patients uncritically reviews the literature without a sufficient standard for what is adequate tricyclic treatment. For example, they quote a study by Stern et al. on patients with a history of "never responding to tricyclics" who subsequently responded to bupropion. However, there were no criteria for adequate tricyclic treatment, and patients given as little as 75 mg of amitriptyline were declared nonresponders. Thus, it is not surprising that Pohl and Gershon conclude that many tricyclic nonresponders will respond to new antidepressants, despite the fact that to date there have been no prospective studies of the efficacy of a "new" antidepressant in patients who have failed to respond to therapeutic plasma levels of tricyclic antidepressants. An uncritical enthusiasm for "new" drugs can lead to other types of unwarranted conclusions; for example, in the same chapter the authors conclude that in general the side effects of nomifensine tend to be mild and either less frequent or less severe than the side effects associated with tricyclics. The authors note that this conclusion is based on treatment of only 1,000 patients, but there is not sufficient appreciation that new medications may have undiscovered substantial risks that will become apparent only when the drug is used more extensively.

A different type of problem exists in Prange's chapter on the use of $T_3$ as an adjunct to antidepressants. Prange's review of the literature is fair, and he dutifully notes that the relatively few studies of the use of $T_3$ have been single-blind and that interpretation of the results is made difficult by variations and criteria for diagnosis and for outcome. In addition, the only "double-blind" study involved just 12 patients. Despite this paucity of data, Prange concludes that when $T_3$ is added to tricyclics, approximately two-thirds to three-fourths of patients will respond and that this phenomenon pertains equally to both sexes and to unipolar and bipolar forms of depression. Given the available data, such definitive conclusions would seem to represent an advocacy for $T_3$ rather than a balanced consideration of the evidence. The worst offenders in this regard are Ayd and Zohar, in their chapter on psychostimulant therapy. Essentially they cite 12 cases reporting the beneficial effect of stimulants as an adjunct to tricyclics in treatment-resistant patients. Nonetheless, they conclude that clinicians have treated an "indeterminate" number of treatment-resistant patients with combined tricyclic-methylphenidate therapy and that they have learned that *d*-amphetamine or methylphenidate in modest doses can be an "effective and safe therapy for depressed individuals between 60 and 90 with all types of medical problems." Frankly, I do not know whether these medications are useful or not, but I think it would be hard for a nonbeliever to come to Ayd and Zohar's conclusions about efficacy or safety from the available data.

Not all of the chapters on adjunctive treatment are permeated with bias; specifically, the contributions on sleep deprivation, the role of estrogens, and the use of reserpine represent balanced, concise reviews of the available data.

Despite its flaws, this is a reasonably good book and certainly a worthwhile reading project if for no other reason than to emphasize to the clinician that if the proven treatments for affective disorder (tricyclics, MAOIs, and ECT) are used adequately, then the number of patients who are truly treatment resistant will be quite small indeed.

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## CLINICAL NEUROBIOLOGY

**Humors, Hormones and the Mind: An Approach to the Understanding of Behaviour,** *by Bernard T. Donovan. New York, Stockton Press, 1988, 281 pp., $90.00.*

This book by a single author summarizes the field of psychoneuroendocrinology and its relationship to behavior in a nondogmatic way. It is a product of the European academic tradition, in which one expert presents wide knowledge and understanding of an entire field. Single-author books run the risk of being one person's view of the world; however, the reader benefits from getting an integrated view at least. The field of psychiatry has moved in the last decade with astounding speed, leaving integrative efforts just short of being out-of-date. If presented well, overviews are invaluable in a rather fragmented and rapidly changing scientific world.

Donovan's lonely heroic quest has produced a very readable, well-written piece of work. The author apologizes in his preface for the "oddities of grammar, punctuation and spelling" that may have occurred when he used quotations from other sources, but, for the U.S. reader, the British idiosyncrasies in spelling (e.g., "behaviour") and punctuation are not offensive. I believe that the scientific community will tolerate them. As the author points out, the locus ceruleus and ACTH play a role in how much we fail to extinct old behaviors or hang on to our cultural heritage and prejudices.

The book begins with an introduction describing the conceptual development of the four classical humours into the present-day view of how hormones, neurotransmitters, neuromodulators, and co-released peptides affect behavior. Particular emphasis has been given to the brain as the source and target of these hormones.

In the second part, the author describes the different compounds he calls humors: the neurotransmitters, the traditional hormones, the neuromodulators, the neuropeptides, and releasing factors. He also describes the role of these humors on the immune system.

The third part, How the Humors Affect the Mind, deals with how these humors relate to the physiology of behavior: emotion, the senses, personality, aggression, eating and drinking, the immune system, stress, learning and memory, intellect, and masculinity and femininity.

This book gives a historical perspective as well as the state of the art in the year 1987. I read about the late Curt Richter, the father of chronobiology, who in 1943 observed that adrenalectomized rats showed preference for sodium salts but not for other chlorides, but I did not find any references to the contributions of I. Arthur Mirsky, one of the fathers of psychoneuroendocrinology. I found a reference to the potential interactions between the dopamine and noradrenaline systems but no reference to posttraumatic stress disorder (PTSD). PTSD was apparently of interest to the British only in the 1920s and 1940s.

The references are well chosen, with a good representation of European contributions but without selling Americans short. The complaint of many European scientists that their colleagues in the United States tend to quote only Americans does not apply to this author in reverse. Although his understandable preference for British scientists does occasionally influence his evenhanded approach, Donovan points out some areas of promise for future research.

The third section is somewhat uneven, which seems to result from his subdivisions. The growth of science may not be as organized as the author's material.

Overall a pleasant, well-written overview of exciting developments, this book may be attractive to the layman as well as to the professional. I believe that this book will be of use to psychiatrists, endocrinologists, medical students, psychologists, behavioral neurologists, and science writers for the next few years at least.

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**Selected Models of Anxiety, Depression and Psychosis,** *edited by P. Simon, P. Soubrié, and D. Wildlocher. Basel, Karger, 1988, 194 pp., $119.50.*

As the title promises, this book offers the reader a series of scholarly reviews of selected animal models of major psychiatric syndromes. This book is not likely to captivate the clinician looking for a quick introductory overview of current animal models in psychiatry. It should, however, be of considerable interest to the clinician or researcher looking for sophisticated reviews of the selected topics.

Major models discussed include learned helplessness, stimulant-induced behavioral sensitization, the fear-potentiated startle response, olfactory bulbectomy, aversive behavioral responses, social interaction as a test of anxiety, and nootropic drugs in dementia. The chapters are authored by investigators with hands-on appreciation of the strengths and limitations of the research being reviewed, lending authority to the text and bibliographies. The authors have effectively incorporated their figures and summary tables. Individual chapters are followed by thoughtful critiques contributed by clinically oriented commentators. The consistency in format and style across the individual chapters enhances the readability of the volume.

Several broad theoretical issues about the validity and applicability of animal models surface repeatedly throughout the book. What is an adequate animal model for a psychiatric syndrome? Are models likely to assist in the development of new treatment strategies, or are most models merely dedicated derivatives of treatments (e.g., anxiolytic or antidepressant medications) discovered by other means? Will the models contribute to an understanding of abnormal pathophysiology implicit in pathological syndromes, or will they be limited to clarifying normal physiological processes (e.g., fear and anxiety)?

There is a compelling balance of caution and enthusiasm in this book. Some of the models have been studied for a considerable number of years, and there is an occasional sense of the researcher defending an established paradigm from the onslaught of new nosological schemes and drugs with newly proven efficacy in the clinic. In other places there is enthusiasm for new understanding of behavioral, anatomical, and neurochemical substrates, with the promise that these models might help us understand treatment resistance and develop new treatment approaches. In summary, this book is to be recommended to clinicians as well as researchers interested in a state-of-the-art assessment of the selected preclinical models.

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## PSYCHODYNAMICS AND PSYCHOPATHOLOGY

**Integration and Self-Healing: Affect, Trauma, Alexithymia,** *by Henry Krystal. Hillsdale, N.J., Analytic Press, 1988, 383 pp., $39.95.*

Alexithymia is the enigmatic and often intractable failure of patients to link feelings to language in such a manner that affect becomes a signal to one's self in the service of self-regulation. Most commonly described in patients with psychosomatic disorders, alexithymia is also part of the generalized affect intolerance that is found in many substance abusers and, as Henry Krystal's previous work has shown, in many patients suffering from severe posttraumatic reactions. Krystal's many decades of study and clinical involvement with the latter kind of patient have provided a clinical perspective not available to those who do not study patients with posttraumatic disorders. He is aware of the extent to which disturbances in affect expression and self-regulation in alexithymic patients are regressive phenomena and not simply constitutional or developmental disorders. *Integration and Self-Healing* is a synthesis of Krystal's clinical, scholarly, and theoretical work with alexithymic patients over several decades.

The book is divided into three parts concerned with emotion, trauma, and alexithymia, respectively. The seven chapters on emotion synthesize major contributions by Krystal and others on affect tolerance and affect regression as central pathological features not only in psychosomatic illness but also in substance abuse and posttraumatic disorders. Krystal expounds the central idea—amplified from his many earlier contributions—that if affects are not capable of being given verbal form, they are less likely to be used as signals to one's self for purposes of self-regulation. The predicament of intolerable affect, then, makes the patient likely to de-differentiate and to somatize, often in a manner that renders the experience of intense affect virtually indistinguishable from the original traumatic situation, i.e., one that seems as though it will never end. Using insights from the work of his late mentor, John Dorsey, Krystal proposes that love rather than anxiety serve as the model affect.

The four chapters in the section on trauma provide a scholarly synthesis of the history of psychoanalytic thinking about trauma. A four-page short story, "The Shawl," by Cynthia Ozick, provides powerful and eloquent counterpoint to the text. The final section, on alexithymia, includes a fine research-oriented penultimate chapter by John H. Krystal and a splendid final chapter distilling Henry Krystal's psychotherapeutic wisdom gleaned over many decades of treating alexithymic patients.

Integration is certainly the hallmark of Henry Krystal's comprehensive and lucid exposition. He offers a synthesis and an integration that are inspired by a deep understanding of psychoanalysis, its theory, its methods, its controversies, and its limits. But the book is also a well-integrated compendium of research bearing on the clinical predicaments being discussed. The volume is a marvelous synthesis reflecting Krystal's dedication to psychoanalysis, to clinical research, and—above all—to the clinical predicament posed by the pathology of his patients. There are 27 pages of references and thorough and fair-minded discussions of scholarly controversies in the text.

This book is both creative and scholarly, comprehensive and personal. It is Krystal's *magnum opus*—a masterful accomplishment, dealing with integration in the process of healing and providing a model for the scholarly integration of psychoanalysis, research, and clinical treatment. It is highly and unequivocally recommended both to specialists in the field and to general psychiatric audiences with some appreciation of psychoanalytic conceptualizations of trauma and psychosomatic medicine.

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**Immaterial Facts: Freud's Discovery of Psychic Reality and Klein's Development of His Work,** *by Robert Caper, M.D. Northvale, N.J., Jason Aronson, 1988, 255 pp., $25.00.*

Can we use another introduction to the work of Melanie Klein? Yes, if it is clearly written and organized in an original way. Dr. Caper's book easily qualifies on both counts and can be readily recommended to the interested reader. As an introduction to Klein's work it complements rather than duplicates Hanna Segal's classic introduction (1).

The book is tightly unified around a central theme: the significance of psychic reality in psychoanalysis. The first part of the book traces Freud's gradual discovery of this dimension, and the second part follows Melanie Klein's course as she takes up Freud's discovery and expands it in directions unimagined by Freud. The continuity of Klein's work with that of Freud is emphasized throughout the book.

The section on Freud's work covers much familiar ground but presents it interestingly as an anticipation of Klein's work. The author first traces Freud's gradual discovery of unconscious fantasy, which eventuated in the conclusion that "as far as the neurosis was concerned psychical reality was of more importance than material reality" (2, p. 34). He then details the developments of Freud's later investigations—psychic agencies built out of identifications, an aggressive instinct as exemplified in an overly harsh superego, and a revised anxiety theory—that prepared the ground for Melanie Klein.

Dr. Caper begins his treatment of Melanie Klein with her groundbreaking extension of psychoanalysis into the treatment of children through the modality of play therapy. This direct exposure to infantile mentation allowed her to expand the field of psychic reality well beyond that of Freud's explorations. Pushing her investigations into earliest infancy, she uncovered an active mental life in the infant of only a few months of age. The earliest instinctual urges are experienced as unconscious fantasies, and these then form the psychic structure of the child. Klein had taken Freud's discovery of the unpredictably harsh superego to heart, and she therefore emphasized the dominance of the aggressive instinct in the infant's mental economy. Full of hateful feelings toward the breast (or mother) as depriving, unable to modulate these through integrating them with its positive feelings, the infant projects them onto the object, which is then experienced as persecutory and is reintrojected as the harsh superego. Psychic reality for Klein is composed of fantasized internal objects, of which a prominent example is this harsh superego. The Kleinian infant is, as it were, caught between a rock and a hard place, having to choose between attacks from without and attacks from within. Not surprisingly, Klein called this the period of the paranoid position.

As the psychic reality of the early infant is one of fragmented drives and internal objects, that of the toddler is one of integration. Now struggling to recognize the giving and depriving mother as one and the hating and the self as one, the child begins to take responsibility for its own hate, to experience guilt, and to make reparation to the mother for its attacks on her. At the same time, because psychic reality is now less dominated by aggressive instinct, the child is able to recognize the mother as she is, less colored by the child's projections. Klein called this developmental stage the depressive position to emphasize the child's mournful acceptance of its destructive potential.

Since all this elaborate development occurs before the period of Freud's oedipal stage, it is not surprising that Klein located the origins of the Oedipus complex much earlier than did Freud. Dr. Caper devotes an interesting chapter to this topic, emphasizing the fact that Klein's account results in much more gender parity than Freud's.

Although Dr. Caper does very well what he sets out to do, it is important to point out what he does not do—what are in fact the book's limitations. The first is the obverse of its merit. There is little indication here of the contradictions and changes in Klein's thought. Dr. Caper's presentation gives an illusion of orderliness that is somewhat at odds with the reality of Klein's development. A second point concerns the distinction between psychic and material reality. Putting Klein up as the most pure of psychoanalysts and, indeed, as less troubled than Freud himself over the intrusions of physiology into the psychic sphere, Dr. Caper simply ignores the active discussion within psychoanalysis of the breakdown of any rigid distinction between psychic and material reality (3). Another point: the author waffles regarding Klein's tendency to find the origin of unconscious fantasy more in instinct than in environment. Compare Winnicott's statement that "unsatisfactory experiences lead to the existence and the strengthening of things or forces felt to be bad within" (4, p. 84), which could not have been made by Klein. Still a further point: although Dr. Caper acknowledges the reservations of Klein's critics regarding the elaborateness of infantile mental life, his omission of any concrete details of Klein's descriptions leaves the reader unable to appreciate what has shocked all those critics.

A final question is at a philosophical rather than a psychoanalytic level. The author's reassurances concerning the empirical-scientific status of psychic reality do not really still my questions about the nature of this sphere. Is psychic reality indeed the empirically discovered and demonstrated realm that the author claims it to be? Do "immaterial facts" enjoy the same status as material facts? Or should psychic reality be considered an elaborate figure of speech, an "as-if" realm of psychic presences, the imagination of which helps to organize and articulate clinical phenomena? Dr. Caper writes that "this inner world is no metaphor for the child, who experiences it as his or her real psychological inside" (p. 13); however, as Roy Schafer has pointed out (5), the fact that children believe in inner presences does not mean that we should erect their concretizations into theoretical structures. To use the language of Gilbert Ryle (6)—who, by the way, should be required reading for all Kleinians—there are many ghosts in Mrs. Klein's machine.

I do not, however, wish to focus too much on what the author does not cover in this book, for what he does cover makes for excellent reading.

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**The Transference-Countertransference Matrix: The Emotional-Cognitive Dialogue in Psychotherapy, Psychoanalysis and Supervision,** *by Robert J. Marshall and Simone V. Marshall. New York, Columbia University Press, 1988, 348 pp., $40.00.*

Psychiatry and psychoanalysis are often referred to as inexact sciences because they are unquantifiable. The Marshalls, both practicing and teaching psychologists and psychoanalysts, present an impressive and innovative measuring instrument to correct this situation.

The book contains eight chapters. In chapter one, transference is defined to clarify the "definitional morass" in the confused literature. The authors consider transference to be variable with antecedents and consequences and subject to the therapist's influence. It is quantifiable by the transference-countertransference matrix. This is a three-factor model: 1) the source of transference, patient-determined or therapist-determined, 2) awareness, reflecting the conscious or unconscious, and 3) differentiation, indicating specific or general. In chapter two the countertransference is treated in graduated relation to transference. Chapter three deals with the interactions of transference-countertransference, as in the life crises of the therapist, their effects on the treatment situation, and their evaluation by matrix studies.

"The unconscious dialogue based on emotional communication," as evident in music, hypnosis, and infant-mother reactions, appears in chapter four. In chapter five, the authors use three schools of thought to illustrate application of psychoanalytic language to the transference-countertransference matrix: Freud's observant orientation, Sullivan's interactive model, and modern psychoanalysis. Chapter six discusses the use of the transference-countertransference matrix in clinical issues and case studies. The authors show that different phases of therapy, interpretation, and intervention can be readily and correctly studied with the matrix. Chapter seven contains the analysis of an obsessive woman over a period of 4 or 5 years using the Sullivanian interpersonal model. The last chapter, "The Supervisory Function," uses the matrix effectively. The epilogue follows with a summary of goals that are fulfilled.

The essential feature of the book is the quantifying matrix that is presented as an operational guide for being alert to the changing interactional field in which patient, therapist, and supervisor function. The authors provide abundant supportive case material in an attempt to integrate the vast influx of new theories, techniques, and research. They mention the stratagems of Freud, Sullivan, Searles, Langs, and others of the many schools of mental health. In each case the matrix is effectively used.

The book is well organized, clearly written, and filled with practical information. The matrix is basically a research instrument. Its major limitation is that its reliability and validity depend on the objectivity, observing capacity, and interpretation of the therapist. Illustrative cases are frustratingly lacking in follow-up evaluation to substantiate the school and the stratagems used. The experienced and well-trained practitioner may find the matrix interesting but, being familiar with the vicissitudes of the transference-countertransference, he or she would have a personal matrix, and that of the authors might not be of enhancing value. The supportive material is much too rich for the fledgling resident. Before using it, the resident would have to become thoroughly acquainted with the imposing writers quoted. Research workers would find it very useful, as would selected patients and the interested public. The book has a rich list of references, a name index, and a workable subject index, although suicide was omitted. In the next printing, consideration should be given to the concepts of conscious feelings and counter feelings advocated by Sandor Lorand, M.D.

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**Psychopathology and Differential Diagnosis: A Primer, vol. 1: History of Psychopathology,** *by Henry Kellerman and Anthony Burry. New York, Columbia University Press, 1988, 250 pp., $30.00.*

This book presents only theories about "functional" psychopathology (in the sense that an organic etiology is unknown or not generally accepted), leaving out of consideration brain lesions or physiological malfunction. The dichotomous pattern is established in the preface: "What emerges historically in . . . [the Age of Enlightenment] is a continual shift from one era to another regarding the causes of psychopathology, with a belief in biologically based causes alternating with an opposing belief that the origin of aberrant behavior lies within the psychological realm" (p. xiii). This volume deals only with the psychological realm. The attitude toward the "opposing" view is illustrated in the following statement from the conclusion of the book:

> As recently as the 1950s, many thousands of patients were lobotomized, inducing in each one a permanent condition usually referred to as the vegetable state. Even as this page is being written, there are places in the world where another bizarre application of the physical approach to treatment is being made: the use of pharmacology to control a person's political orientation and preferences. Most of these methods are now judged to have been primitive and irrelevant at best, and at worst, quite cruel. (p 242)

Such words as these could have been written only by persons who never worked in an emergency room or the admitting area of a mental hospital.

It would appear that the only test of theories of the etiology of pathology included is whether they satisfy some intellectual criteria, not whether or how well they work in practice. One longs for at least one fourfold table from which the practical usefulness of a theory might be calculated. The only experiment contained in the volume is one Adolf Meyer would have called "an experiment of nature." It is René Spitz's observation of physically well cared for but linguistically and emotionally deprived infants. This led to the reform of orphanages and the development of foster home care for homeless children.

The third exclusion from consideration is the changes in physical and intellectual capacities that take place during development. Gesell, McCarthy, Sears, Bowlby, Piaget, Kagan, and many other contributors to knowledge of maturational behavior are not mentioned.

The ancient history section omits mention of the sweeping flows of anxiety seen in the early Dravidian scripts. As everywhere in the book, the brevity imposed limits the exposition. The originators of the theories presented are almost never quoted, so the reader is entirely dependent on the authors' interpretation. In the reference to Rorschach's personality classification, the introversive and extratensive measure is noted, but the more original coartive-dilated measure (1) is not (p. 133). The derivation of the word "anxiety" given (p. 166) does not agree with the *Oxford English Dictionary.*

The book will serve as a stimulus, perhaps, to recall old friends in the literature. It should not be depended on as a secure, and by no means as a complete, history of psychopathology.

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## CHILD PSYCHIATRY

**Critical Issues in the Early Development of Premature Infants,** *by Sibylle K. Escalona. New Haven, Conn., Yale University Press, 1987, 284 pp., $35.00.*

The contributions that several investigators have made to the literature on child development have made it possible for child psychiatrists and health practitioners working with children and their families to be able to appreciate children and their behaviors in holistic rather than in compartmentalized ways.

The present book is actually the result of a thorough, detailed, and meticulous study that Escalona and her team of co-workers conducted among 106 low-birth-weight infants and their relatives, who were methodologically evaluated for 40 months of the children's lives.

To evaluate these children, Escalona and her co-workers devised scales assessing impulse control, structure, accommodation, didacticism, focused attention, frequency of conflict, and intensity of maternal involvement, plus a final assessment of the developmental course of each child.

The children were mostly of low socioeconomic backgrounds, a fact that did not interfere with the remarkably high frequency of contacts that the researchers maintained with the families and children investigated.

Children who participated in this study, located in a neonatal intensive care unit, had a birth weight of less than 2500 g, had a gestational age of less than 36 weeks, or were small for their gestational age according to established criteria. In addition, for obvious reasons, all of the mothers were reasonably well able to communicate in English.

The first three chapters of the book cover the method and the setting for the study. These three chapters abound in graphs and exhaustive explanations of the researchers' strategy, leaving no area of significance or relevance uncovered for the purpose of the study.

The second part deals with the results that were obtained by analyzing what the author considers the "intact group," followed by a well-placed interlude giving clinical vignettes of six children from this group.

The final part gives the results for the "deviant" group with a second interlude giving vignettes of five children, two from the "neuro" group and three from the "behavior" group.

The final chapter, "Concluding Comment," should be read by anyone interested in research on developmental issues. It provides the interested reader with a thorough understanding of the state of the art in this type of research and data analysis.

In summary, this book is well conceived, timely, and relevant, and it contains much information not only about children who are considered to be at high risk but also about how to design effective methods to analyze the behavior of children as they separate from their mothers and enter social life. This book should be added to the many relevant contributions in the literature of child development, normal or otherwise.

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**Psychotherapeutic Strategies in the Latency Years,** *by Charles A. Sarnoff, M.D. Northvale, N.J., Jason Aronson, 1987, 360 pp., $37.50.*

**Psychotherapeutic Strategies in Late Latency Through Early Adolescence,** *by Charles A. Sarnoff, M.D. Northvale, N.J., Jason Aronson, 1987, 264 pp., $30.00.*

These books are welcome sequelae to Dr. Sarnoff's authoritative book *Latency,* published in 1976 (1). Concepts presented in the earlier work are amplified, providing a fresh approach to understanding and helping children. The author weaves a fabric of knowledge that gives careful consideration to developmental change in the context of culture and relationships. In this era of increasing focus on biological considerations in child and adolescent psychiatry, it was a happy experience for me to renew my acquaintance with the psychological structure we call latency. These works stimulate not only a healthy inquisitiveness about etiology but also lead to a fuller understanding of complex developmental processes. The use of clinical vignettes to illustrate psychological concepts and treatment strategies contributes much to their readability.

Latency is defined both as the age period from 6 to 12 years and as a psychological state in which dynamic defenses allow "a complex reorganization of the defensive structure of the ego." The first half of *Psychotherapeutic Strategies in the Latency Years* provides us with a skillful integration (drawing on Piaget and psychoanalytic theory) of cognitive, physiological, and psychological maturational changes. The shift from the child's use of evocative symbols representing unconscious content to the adolescent's facility with communicative symbols is emphasized. Dr. Sarnoff is a master at clarifying psychodynamic concepts; he helps us understand how symbol formation is a cornerstone of latency—these symbols conceal, yet represent, repressed forbidden drives.

Can latency survive? How powerless are today's children? Sarnoff writes, "There is no way out, in reality, for this celibate soldier-dwarf" (*Psychotherapeutic Strategies in the Latency Years,* p. 6). Given recent concerns about a marked increase in the number of children given diagnoses of conduct disorder, the reader may wonder if today's children don't feel more empowered and whether the structure we call latency is weakening. One wishes that Dr. Sarnoff had commented on the extent to which latency is being stressed and modified by the explicit images children view on television and movie screens. He does point out that latency is a psychological "structure" that varies in its intactness, and he notes that repeated exposure to sexual stimulation may predispose the child to overt sexual expression rather than the development of psychological defenses and masking symbols.

Chapter 11 of *Psychotherapeutic Strategies in Late Latency Through Early Adolescence* makes an important contribution to our understanding of late adolescence. Dr. Sarnoff describes the shift to reality-oriented, goal-directed behavior and cites separation milestones such as high school graduation and pairing off with a sexual partner. He shares his view of love and marriage: "Love in courting and in marriage consists of benevolence towards the partner and pleasure derived from the partner with justice all around." Sarnoff makes the point that for emotionally immature people, sexual intercourse and marriage are superficial aspects of life likely to exacerbate neurosis and other mental ills.

Approximately half of each volume focuses on psychotherapy. These sections are useful guides to assessment and treatment. They give the reader valuable techniques and therapeutic strategies that deserve careful consideration. The fuller understanding gained from these books of how effective psychotherapy depends on knowledge of complex developmental processes not only will increase the therapist's effectiveness but should enhance the personal satisfaction derived from these efforts. Practical therapeutic techniques are presented, spiced with occasional bits of humor that increase the reader's pleasure and enhance understanding. Dr. Sarnoff describes ways of dealing with perplexing moments in therapy that, although difficult, are opportunities for insight. It became clear that the therapist who possesses the knowledge and skills so beautifully presented in these books will be more effective in providing patients with emotional and cognitive growth. However, these are expensive therapeutic endeavors, and we see many children who lack adequate sponsorship and who have no access to such skilled therapists. How are we to help them?

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**Learning Disorders: An Integration of Neuropsychological and Psychoanalytic Considerations,** *by Arden Rothstein, Lawrence Benjamin, Melvin Crosby, and Katie Eisenstadt. Madison, Conn., International Universities Press, 1988, 381 pp., $45.00.*

There are two important things to know about this book. First, it attempts a very timely and extremely important task—that of describing the interrelationship of symptoms of psychiatric disorders and the manifestations of learning disabilities. Second, and most unfortunately, it is generally 10 years out-of-date both in its understanding of learning disabilities and in its coverage of the literature on the relationship between psychiatric disorders and learning disabilities.

Taking the worst first, only a few of the book's more than 300 references were published after 1979. The most recent work on learning disabilities cited are one paper published in 1982 and a review chapter from 1983. On the interrelationship of psychiatric disorders and learning disabilities the picture is equally bleak. There are no references to the important work that has been done in the past 10 years exploring the prevalence of learning disabilities in psychiatrically diagnosed populations, and there is no mention of the work done exploring psychiatric disorders in children who are identified as having learning or language disabilities.

Specifically, the authors have failed to include any consideration of the work of Beitchman, who proposed a model of neurodevelopmental immaturity to account for both learning disabilities and psychiatric risk. This model was first published in 1985. Furthermore, the authors fail to discuss the work of Baker and Cantwell, who explored language disability and its relation to psychiatric disorders, and the work of Gualtieri, who studied language disorders in children already referred for psychiatric services.

In the past 10 years, research on learning disabilities has widened from behavioral assessment of the expression of the disability to include investigation of neuroanatomy (for example, the work of Galaburda and Kemper), and exploration of a genetic basis for a variety of learning disabilities (the work of Smith, Pennington, Lubs, and Wood). In this recent work, family studies have uncovered evidence for the presence of both learning disabilities and psychiatric disorders in the families of children identified as having learning disabilities. The crucial problem for the present volume is that the authors' central thesis is not measured against this current knowledge.

The authors believe that children may arrive at learning disabilities by means of a psychiatric disorder. That is, a child may have trouble learning in school because of a disordered relationship with his or her mother. This is the first of the four categories of learning disability the authors outline, learning disorders of primary psychogenic etiology. The other three are learning disorders of primary neuropsychological etiology, admixtures of psychogenic and neuropsychological etiology, and, finally, learning disorders attributable to intellectual limitations. Despite the authors' presentation of 12 specific subtypes in these four broad causal categories, they are mainly interested in considering the issues of learning disorders of primary psychogenic etiology and admixtures of psychogenic and neuropsychological etiology.

What do the authors miss by ignoring the past 10 years of literature in the field? Well, for one thing they do not address the possibility that the child's emergent emotional and social self does not cause problems in and is not disrupted by problems of the neuropsychological realm of language, speech, and related motor functions. They do not consider that the child's immature or dysfunctional brain organization may include both an immaturity of or deficit in brain functions needed for school learning and an immaturity of or deficit in brain functions subserving social interaction. Moreover, and most important, few theorists share the authors' belief that specific learning disorders could be engendered by maladaptive family interactions.

The most valuable aspect of this book is the set of case studies and treatment reports forming chapters five and seven. The authors' effort to integrate psychosocial therapy and learning disability remediation is impressive. It is in these chapters that the authors' grasp of the complexity of the developmental phenomena comes clear. They now need to investigate the validity of their subtypes and work within the current framework of the field. There may well be psychological factors that, to paraphrase the authors, eventuate in a learning disability. This should be a research question.

Although the authors overuse the word "polemical" in chapter three, the situation they've applied it to remains a core problem: psychiatrists and neuropsychologists do need to develop a shared understanding of the range of problems of children labeled as "learning disabled."

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**Treating Troubled Adolescents: A Family Therapy Approach,** *by H. Charles Fishman. New York, Basic Books, 1988, 336 pp., $24.95.*

This tightly written volume lives up to the second part of its title. The family therapy in the volume consists of six treatment episodes conducted, explained, and annotated by a true master. These vignettes are organized according to a four-point model—contemporary developmental pressures, history, structure (including closeness and distance among family system elements), and family process, with or without the therapist's interactional contribution.

The author emphasizes the necessity to identify the "homeostatic maintainer," who is believed to be the key to dysfunctional patterns and, therefore, for change, especially through brief therapy. Among key maneuvers in this therapeutic endeavor are establishing appropriate boundaries, enacting the basic conflict, balancing the system by taking sides, and, finally, searching for competence within the system.

Adolescence is viewed as a psychosocial stage as defined by Rutter. The author claims that the most powerful change-producing intervention for adolescents is therapeutic work with their families. I venture that a similar argument could be made for peer group therapy, especially with specific problems like addiction or other sociopathic behaviors. However, in this treatise the disturbed adolescent is viewed as a signal of family malfunction or stagnation, whereas influence and impact from the larger context (peers, the community, etc.) are accounted for only briefly in the excellent epilogue.

Although the therapeutic work is of the highest caliber and in most examples very successful, the selection of case material seems rather idiosyncratic. There are troubled adolescents in all of the families, but they are not always the complainers in the examples selected.

The first example, however, of a family with a delinquent, represents a rather typical situation. The therapeutic efforts in this case include emphasis on the extrafamilial context by ensuring contacts with wholesome peers and adults, as practiced, for instance, at the Wiltwyck School for Boys, where some of the earliest work with delinquents and families was done under the auspices of Salvadore Minuchin.

The example of the "runaway" adolescent in the next chapter, however, is not well chosen; the child is not the typical runaway but left home at the "invitation" of her parents. This is, of course, not rare among runaways, but in this instance the adolescent just moved a short distance to live with her boyfriend. She was not available for treatment at first but eventually agreed to participate in family therapy. Like almost all treatment described in this book, it was carried out in a masterly and successful fashion.

The next chapter, "Treating the Violent Family: First Do No Harm," represents a more typical problem of a violent father and husband who drinks too much on weekends. As the treatment process unfolds, appropriately facilitated by the therapists and the supervisor-consultant behind the screen, the focus shifts from violence or threat of violence by either the father or the older son to the mother's passivity and the task of how to get her to express herself and side with her husband rather than her children. This is accomplished by establishing the parents as a separate entity or subsystem in the family, often a necessary goal in family treatment with a problem adolescent.

The chapter concerning incest seems to focus rather narrowly on the husband-father as the culprit, but otherwise the emphasis in the treatment process on establishing effective boundaries is well taken. Affirming the generation boundary is critical, but considering it vertical strikes me as odd because we usually visualize it as horizontal in genograms.

The case presentation of an adolescent suicide attempt again seems rather atypical in that the patient belongs or is expected to belong to two reconstituted post-divorce families, not an uncommon example per se. But treatment of families after an accomplished suicide is, unfortunately, a more urgent problem.

The next chapter, on disabled adolescents, also seems a rather strange selection. Despite the author's vast experience with psychosomatic and chronic illnesses, the example presented is that of a Swedish family with a mildly retarded daughter. This case, as well as some of the other illustrations, highlights the need for continued care or follow-up, even at great intervals, which the author compares to recurrent visits to a family physician, even though one particular disease may have been cured or a crisis resolved.

The single parent example also seems not to be the most typical in that it deals with a divorced mother who is still in touch with the children's father. The so-called chief complaint concerns the oldest daughter, an adolescent who is concerned not only for herself but for her siblings because of the mother's guidance, or lack of it. This is represented by a very chaotic household situation, including nine animals. Again, the therapeutic process is deft and well presented as well as effective, but to me a typical single-parent family is a never-married mother with one or more children who is usually immature (likely a teenager herself when she became pregnant the first time) and eventually will be beset by many extrafamilial problems, all too well-known. Adolescents in such an environment are at great risk not only for repeating the mother's history of teenage pregnancy but also for delinquency, drug abuse, etc.

The last chapter, "Couple Therapy," includes two teenage children, but the main problem in the family is the "adult adolescent," the mother, a chronic anorexic who intermittently starves and purges herself into electrolyte imbalance to a serious and life-endangering degree. Again, we are presented with an excellent piece of treatment, freeing up both parents from their lopsided bondage: the mother who feels neglected and disregarded and the father who feels unable to cope with his own resentment and anger over the mother's vindictive illness behavior. The father involves his children as caretakers and watchdogs for the mother, which further undermines her self-image. The key to therapy, however, has to do with removing the mother's parents, so to speak, from the scene. In the author's words, "One layer had to be peeled after another." Then the children, who are the homeostatic maintainers, are encouraged and given the freedom to pursue their own development, while the couple is helped to become interdependent rather than independent, although that option is raised on both sides as a possible solution.

In summary, we are presented in this book with an excellent treatise on how to carry on family and couples treatment in families with adolescents, but we are not presented with a spectrum of some of the most typical problems besetting adolescents, as suggested in the first part of the title. This criticism is met in the epilogue, in which the author addresses the broader conditions of adolescence today, pointing out the decline in morality and value guidelines for young people in the Western world and yet emphasizing the need for hope that this larger context will improve. Without such hope, adolescence indeed is a grim experience. Family and couples therapy as presented here is an example of how systems can be improved through participation and a systemic initiative.

This book should prove useful to anybody interested in or preparing to engage in treatment of adolescents with or without their families.

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**X-Linked Mental Retardation 3,** *edited by John M. Opitz, Giovanni Neri, James F. Reynolds, and LaVelle M. Spano. New York, Alan R. Liss, 1988, $120.00.*

This volume comprises the proceedings of the September 1987 Third International Workshop on X-Linked Mental Retardation, which has also been published in its entirety in the *American Journal of Medical Genetics.* The subject is certainly one that psychiatrists, especially child psychiatrists, should be conversant with. Between 4% and 20% of mentally retarded individuals have a cytogenetically diagnosable defect called fragile X. Female carriers of the fragile X gene, including mothers of fragile X boys, may have behavioral abnormalities. Autistic children, according to some reports, also have a significant incidence of the fragile X abnormality, although more recent reports cast doubt on this claim. The fragile X abnormality is reasonably easy to diagnose cytogenetically in blood samples and provides powerful information for prognosis and genetic counseling.

The present volume is extraordinarily comprehensive, including more than 70 chapters on every conceivable aspect of the syndrome. Psychiatric and behavioral aspects take up only a small part of the volume. The book is a must for libraries but is useful specifically only for specialists because focused psychiatric reviews of the fragile X syndrome are available for general psychiatrists.

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**Childhood Schizophrenia,** *by Sheila Cantor. New York, Guilford Press, 1988, 193 pp., $25.00.*

This provocative book is offered by Dr. Cantor as a reflection of her own clinical bias. She believes that "childhood schizophrenia deserves to be conceptualized as a distinct clinical syndrome." The diagnosis of childhood schizophrenia was not recognized in *DSM-III,* and she made efforts to reaffirm its validity in the psychiatry literature (1, 2). She advises that children with schizophrenia are currently diagnosed according to the same criteria as are applied to adults and that this is too limiting. In her concept, Kanner's definition of infantile autism should be included in a classification of childhood schizophrenia.

It may be difficult to differentiate between the *DSM-III-R* diagnostic category of pervasive developmental disorders and Dr. Cantor's description of childhood schizophrenia. *DSM-III-R* describes pervasive developmental disorders as characterized by "qualitative impairment in the development of reciprocal social interaction, in . . . verbal and nonverbal communication skills, and in imaginative activity." Activities and interests are markedly restricted and frequently stereotyped and repetitive. Associated conditions include developmental delay or distortion in the areas of intellectual skills; language comprehension and speech production; posture and movements; patterns of eating, drinking, and sleeping; and responses to sensory input. Dr. Cantor, in her study of childhood schizophrenia, presents data on abnormalities in sleeping and feeding behaviors and early motor, social, and cognitive development in children she diagnosed as "pre-schizophrenic." She goes a step farther in chapter five, where she presents an investigation of possible physical signs of pre-schizophrenic children. Many signs initially appeared significant, but most prevalence rates regressed toward the mean with larger sample sizes.

Dr. Cantor also reports that adult "negative symptoms" of the residual phase of schizophrenia can be identified in the category of childhood schizophrenia; *DSM-III-R* reports that these can be identified in the category of pervasive developmental disorders. According to *DSM-III-R,* substantive research suggests that pervasive developmental disorders are unrelated to adult psychoses and that the additional diagnosis of schizophrenia can be made only in rare instances in which prominent delusions or hallucinations meeting the criteria for schizophrenia are documented. Dr. Cantor, in contrast, believes that schizophrenic children go undetected and fall into the category of mental retardation.

In her final chapter, "The Case for Early Identification and Treatment," she describes the design of an appropriate therapeutic milieu. She states there is some agreement that schizophrenia at any age is an ego deficit syndrome and that internalization of self-regulation (i.e., autonomous ego function) is the long-term objective of intensive psychotherapy with schizophrenic children. This also reflects her clinical bias, and psychiatrists who do not share her views will find her assumptions difficult to fathom and accept. *DSM-III-R* defines autistic disorder as a severe form of pervasive developmental disorders, autistic disorder, and a separate entity from schizophrenia; Dr. Cantor would include it in her diagnostic category of childhood schizophrenia, leading to overlap of terms and clinical descriptions.

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## COGNITION

**Psychodynamics and Cognition,** *edited by Mardi Horowitz. Chicago, University of Chicago Press, 1988, 389 pp., $27.50.*

Despite the injunction, "Come, let us reason together," too few books help us to that goal. *Psychodynamics and Cognition,* the result of MacArthur money and Horowitz's vision, is one of those rare books. It follows in the tradition of the Nebraska Symposiums on Motivation, a gathering of differing experts presenting ideas in a setting that provides opportunity for response, counter-response, and presentation of follow-up.

The book is predicated on the idea that psychodynamic theory and cognitive psychology are separated by a common language. The first two sections, Consciousness and Unconscious Formative Processes and A Clinical Psychodynamic

Perspective, are about psychiatric work rather than presentations of data and include Horowitz's useful, simple, but not simplistic abstractions from clinical experience, which are essential to the process of theory building. Refreshingly, despite his psychoanalytic background, he does not start with, "In 1900 Freud said . . . " but, rather, searches for a new language and provides us with "a trial lexicon of terms for a dialogue" between the fields of psychiatry and psychoanalysis. It remains to be seen, however, whether "schemata" serves us better than "mental representations."

The remaining three sections attempt, as Erdely's contribution states, to "combine the vigor of the clinic and the rigor of the experimental laboratory" or, in Luborsky's words, the "complementary assets and liabilities . . . [of] the naturalistic-clinical and the laboratory-experimental" research styles. Shevrin presents data linking meaningful subliminal presentations with event-related potentials derived from the EEG. Marcel, arguing in response, states that physiology "has no intentionality, no meaning, no symbolisms. The two domains are not commensurate and, therefore, cannot be used to converge." Shevrin responds, Marcel answers, and Jackendoff comments. Good minds at play, illustrating George Gaylord Simpson's adage that science is organized play for grownups.

Luborsky's discussion of momentary forgetting focuses on a series of specific clinical examples from treatment, such as, "Now I've lost the other thing I was going to say," and their relationship to the core theme of conflicting relationships. Spence and Baars offer stimulating variant views. In the final section, on conscious experience, papers by Singer and Zajonc, despite reference to Proust, Joyce, and Woolf, curiously omit the early work of phenomenologic experimentalists such as Silberer and Varendonck, particularly surprising in a volume including students of David Rapaport. The book closes with a summary chapter by Horowitz.

This book deals with the theory and pursuit of our science, not with the practice of our art. It holds the promise of psychiatry and our patients' future. It is a book for those who like to think about what we do as well as those who do it. It provides us with the too rare shock of old ideas newly reexamined.

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**Thought Without Language,** *edited by L. Weiskrantz. New York, Clarendon Press (Oxford University Press), 1988, 509 pp., $85.00; $55.00 (paper).*

Wittgenstein once wrote that "thinking" can be defined as a kind of "speaking in the imagination, a 'speaking in the head' " (1). This book, a compendium of a 1987 international conference of the Fyssen Foundation on the cognitive abilities of animals, preverbal infants, and humans with neurological lesions affecting language competence, challenges the notion that thought requires language.

It is now clear that infants quickly develop the ability to respond intelligently to their visual environment. This developmental process is revealed through a series of cognitive studies detailed in the book. Almost at birth babies are able to discern complex visual features. Gestalt-based recognition and physical "object constancy" seem to be well established by 7 months, and the creation of higher-order categories of objects is in full swing by 10 months. Piaget's developmental scheme seriously underestimated the preverbal infant's intellectual abilities because the infant does not have motor abilities that readily demonstrate intelligence.

From animal studies we learn that even newly hatched chicks have a sophisticated apparatus capable of recognizing and remembering the image of their mother hen and other complex visual objects that have been "imprinted." Pigeons go even farther and do impressively well in developing the ability to categorize novel sets of objects: if presented with the photograph of a single oak leaf, the pigeon can be trained to pick out pictures of other oak leaves when presented among photographs of non-oak leaves. This type of inductive inference is out of the reach of our best artificial intelligence computer systems to date.

If infants and animals are capable of very complex information processing, what, if anything, does language make possible, cognitively speaking? A fascinating chapter by Premack indicates that language training allows apes to successfully perform visual analogy tasks if and only if they are subjected to language training that includes the words "same" and "different." Leslie argues that language allows children to pretend; creating imaginary worlds is critical for problem solving by humans of all ages. A chapter by Gazzaniga states that superior functioning of the right hemisphere of commissurotomy patients on certain visual-spatial tasks was robust primarily for those patients who had some sort of right hemisphere language ability. Thus, language capabilities do seem to galvanize cognitive competence under many conditions. However, a captivating first-person account by a dyslexic mathematician, who describes his own use of visual and tactile imagery to accomplish complex mathematical reasoning, reaffirms that thinking—indeed, brilliance—can be achieved without words.

Certain themes are shared by chapters that review lesion studies in humans. One is that the old distinction between right and left hemisphere cognitive tasks is plain wrong. Practically all cognitive processes require the complex interweaving of neurobiological processes on both sides of the callosum. Second, it is clear that the cerebrum is organized as interacting modules, so that discrete neurological lesions generally will have very delineated cognitive effects; the confusing thing is that the spatial location of functional modules for different individuals seems to be very variable. Third, cognitive and psychophysiological studies suggest that the main effect of many neurological lesions is to block the output of a cognitive process from reaching consciousness rather than knocking out the process itself. For instance, the brain of a cortically blind patient is responsive to visual information, and the brain of the prosopagnosia patient recognizes familiar faces even when the person cannot. Consciousness (and the induction of speech responses) seems to be an optional final stage for these cognitive systems.

I remain skeptical that thinking can readily be separable from language if "thinking" is defined along the lines of "willful pondering about something." As best I could make out, those instances of thought without language most clearly delineated in the book pertain to the intelligent perception and categorization of objects. These processes in humans ordinarily occur more or less automatically, i.e., without willful reflection. Perhaps only those individuals with exceptional talents—artists, mathematicians, musicians—find ways to represent ideas when actively pondering and reflecting that do not rely on linguistic expressions and thereby are able to escape the constraints of thinking only about that which one can "say" to oneself.

Although psychiatric research now assesses itself according to the brain images it produces, I hope it will still allow a place for the mind. Psychiatric illness invariably alters the categorization of experience as much as it alters neurotransmitter levels. Reviewing this book has reminded me of the impressive strides made in cognitive science and their potential relevance to our field.

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*Reprints of Book Forum reviews are not available.*

# Letters to the Editor

## Is the Carbamazepine-Phenelzine Combination Safe?

SIR: Carbamazepine is becoming increasingly popular as a prophylactic and therapeutic agent in the management of affective disorders (1). As its use increases, it is likely that it will be used in combination with a variety of psychotropic agents, including tricyclics, phenothiazines, lithium, and monoamine oxidase inhibitors (MAOIs), and it is imperative that clinicians know whether or not such combinations are safe. There have been a few reports of a marked rise in carbamazepine levels, with toxicity, as a result of the combined use of carbamazepine and isoniazid, which is an MAOI (2, 3). The possibility that this interaction may occur with all MAOIs was negated by Joffe et al. (4), who observed no interaction between carbamazepine and tranylcypromine (which belongs to the nonhydrazine group of MAOIs) in their patient. However, there are no reports to indicate whether this property is shared by others in the hydrazine group of MAOIs, which includes isocarboxazid and phenelzine, or is unique to isoniazid. We report here a patient who was treated with a combination of carbamazepine and phenelzine without induction of toxic blood levels or serious adverse effects.

> Ms. A, a 70-year-old woman with poststroke depression, had been resistant to treatment with carbamazepine alone and in combination with lithium and tricyclic antidepressants. Initially, she was treated with a combination of 400 mg/day of carbamazepine and 150 mg/day of dothiepin hydrochloride; her mean±SD serum carbamazepine level during this period was 47±2 μmol/liter (normal range=30–50 μmol/liter). Since she did not respond to this, lithium, 800 mg/day, was added; her mean serum carbamazepine level for the following 4 weeks was 46±3 μmol/liter. Because of a lack of response, lithium and dothiepin were stopped, and after a 10-day washout period, phenelzine, 45 mg/day, was added. Ms. A showed significant improvement in her mood state with this combination, and there were no adverse effects noted. Her carbamazepine levels remained essentially unchanged during this period.

This case indicates that phenelzine, unlike isoniazid, does not produce a marked rise in carbamazepine levels or toxicity. Nonetheless, because there is some evidence to suggest that both the hydrazine and nonhydrazine groups of MAOIs cause hepatic microsomal enzyme inhibition, which is the principal route of carbamazepine metabolism (5), further study of the potential pharmacokinetic interaction between carbamazepine and MAOIs is needed before any firm conclusions are drawn.

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## Affective Disorder Following Use of Phenylpropanolamine

SIR: One of us (P.F.G.) previously reported a case in which psychotic and mixed affective symptoms followed ingestion of phenylpropanolamine and persisted longer than a week after cessation of the medication (1). The patient required treatment with lithium and a neuroleptic. We now report a second patient with affective symptoms that persisted after discontinuation of phenylpropanolamine.

> Ms. A, a 37-year-old married woman, came to the emergency room with a 1-week history of racing thoughts, lack of sleep without fatigue, rapid speech, irritable and expansive mood, paranoid delusions, and auditory hallucinations. Two days before the onset of symptoms, she had been given a diagnosis of sinusitis and had been prescribed cephalexin and a long-acting preparation containing 75 mg of phenylpropanolamine and 600 mg of guaifenesin to be taken twice a day. Her personal and family histories showed no psychiatric problems. She had previously taken phenylpropanolamine preparations in lower doses without difficulty.
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> A mental status examination showed pressured speech, overly inclusive and tangential responses, anxious mood with elevated and expansive affect, and delusions about the devil. There were no active hallucinations. Results of a physical examination and screening laboratory studies were normal.
>
> Ms. A was admitted to the hospital, and the antibiotics and decongestant were discontinued. No psychotropic medications were given. The delusions and hallucinations resolved, and the patient soon developed normal sleep and activity patterns. A head CT scan, with contrast, and a sinus X-ray series were both normal. The patient was discharged and outpatient follow-up was arranged.
>
> Ms. A soon noted early morning awakening, racing thoughts, increased activity, depressed mood, crying spells, and return of the paranoid delusions. These symptoms persisted for 3 weeks. She was readmitted, started taking lithium carbonate and fluphenazine, and rapidly experienced a return to normal mood and sleep as well as

resolution of her psychotic symptoms. The fluphenazine was discontinued without a recurrence of symptoms.

Phenylpropanolamine has long been used as a nasal decongestant, in doses of 25–45 mg every 4–6 hours and a maximum daily dose of 150 mg. Recently, it has been used as an anorexiant, in doses up to 75 mg and a recommended maximum daily dose of 150 mg. Long-acting decongestant formulations are also now available, in 75-mg doses, to be taken at 12-hour intervals. In previous reports (2–4), psychotic symptoms followed ingestion of phenylpropanolamine in more than the recommended dose, and symptoms resolved within several days of discontinuing the drug. Phenylpropanolamine causes CNS stimulation; this is explained by the close structural similarity between phenylpropanolamine and amphetamine (5).

Since this is the second case of a persistent affective disturbance following phenylpropanolamine ingestion that we have seen, we propose that there is a relationship between phenylpropanolamine and induced affective disturbances. In view of the over-the-counter availability of this medication and the recent availability of larger-dose formulations of decongestants and anorexiants, it is important that patients with affective disturbances be closely questioned regarding ingestion of these substances, especially the higher-dose formulations.

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## Change in Response to Pemoline at Puberty

SIR: While working as a psychiatric consultant at a university health service, I encountered a sophomore student who had been continuously treated for attention-deficit hyperactivity disorder with pemoline, 112.5 mg/day, since he had been in the third grade. I present this case to illustrate that there was an impressive initial pharmacologic response which was followed, when the patient was in the ninth grade, by a permanent alteration in the psychic effects of the medication; i.e., pemoline no longer had the paradoxical calming effect, but caused wakefulness, alertness, and anxiety.

When Mr. A first came to me for a "routine prescription renewal" of pemoline, he was 6 ft 2 in tall, weighed 165 lb, and had a blood pressure of 120/70 mm Hg. He appeared calm and reserved but awkward in relating to me, as if he did not know what to say. He displayed no tics. He was excelling academically, maintaining a 3.8 grade point average.

He is the second of three children. A phone call to his mother revealed that Mr. A underwent the normal neurodevelopmental milestones and had the usual childhood illnesses. She told me that at age 4 he had terrible dreams of "seeing a tiger," which woke him five times each night. The dreams tapered off in frequency by the time he was 5 years old. She described him as an "extremely rude" child, alternating with being overly sensitive. After he began elementary school, the family could not get through a meal without sending Mr. A to his room. He was so unruly that his siblings did not want to play with him. His teachers in the first and second grades were able to keep him within limits, and Mr. A managed to get by. In the third grade his teacher was overwhelmed by him. In class, if someone spoke of the color brown, he would discuss bowel movements, and during the Pledge of Allegiance, he would belch. On one occasion, when given a package of Lifesavers, he pulled the zipper of his pants down and pretended that the package was his penis. Subsequent to this disruptive behavior, he was referred to a pediatrician, who began treatment with pemoline. There was great behavioral improvement. However, in the ninth grade, Mr. A noted a change in the effect of his medication. It woke him up "like coffee." He never told anyone of this transition. I have been unable to locate his medical records because of physicians' retirements, and his school records are unavailable so far.

Over the past 2 years I have slowly tapered the pemoline by 18.75-mg increments; Mr. A now takes 18.75 mg/day. He has been most reluctant to speed up this process, fearing that this would cause a decline in his academic abilities. There is no evidence that his disorder is returning. In fact, he has made some pertinent observations to the contrary, as follows: 1) there will be 10 days to 2 weeks of sleepiness after the dose is decreased, and if he forgets to take his medication, he will sleep all day, 2) his academic performance has not changed, and now, before exams he feels more relaxed and calmer, whereas before he was overly anxious and felt "wired," and 3) he performs in competitive athletic events "more intelligently." He is able to think in a more relaxed way during an event, enabling him to better execute strategies during a race. His times for these events have improved as we have tapered the medication. I hope to have him stop taking pemoline entirely in another few months.

This case documents a spontaneous and permanent change in subjective response to a stimulant that occurred when the patient reached the age at which puberty would be expected. It is believed that two-thirds of children with attention-deficient hyperactivity disorder will outgrow it (1). It would be interesting to determine whether a similar change in subjective response to stimulants at puberty is observed generally in children with the disorder who go on to outgrow it. This would have clinical importance in terms of deciding when, and if, to taper medication.

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## An Atypical Responder to Clozapine

SIR: We write to describe a fortunate outcome for a severely ill female patient who, after 2 years on an inpatient service, finally showed a remarkable response to clozapine. Her clinical picture was quite different from that of the treatment-refractory, negative-symptom-laden, chronic schizophrenic patients for whom clozapine is generally recommended (1). She was the only nonschizophrenic patient studied at our center, and, to our knowledge, there have been no systematic studies describing clozapine trials in patients with nonschizophrenic psychoses, although there is increasing call for such trials (2).

> Ms. A, a 32-year-old Hispanic woman, had a diagnosis of schizoaffective disorder, based on prominent and partially independent affective and psychotic pathology. She had had predominantly affective and borderline symptoms for 3 years before admission to the hospital and had been treated with tricyclic antidepressants, lithium, and carbamazepine. She had had two acute hospitalizations for suicide gestures (overdoses). She was referred to our unit, a specialized milieu for personality disorders; however, she did not respond to psychotherapy and milieu treatment and soon showed unmistakable depressive and prepsychotic symptoms. Treatment with nortriptyline and the subsequent addition of thiothixene, 15 mg/day, for 3 months did little for her. Further addition of lithium did not stem her decline, and she soon manifested a full-blown psychosis with prominent delusions and auditory hallucinations. Diagnostically, she was considered to be psychotically depressed or schizoaffective. When the dose of thiothixene was increased to 40 mg/day, her psychotic symptoms became milder but she developed tardive dyskinesia. Discontinuation of the thiothixene brought her to an acute crisis, with desperate and persistent attempts to kill herself. Finally, ECT resolved some depressive features but worsened her paranoid delusions and hallucinations.
>
> Although Ms. A differed from the prototype patient (a chronic, treatment-resistant schizophrenic patient who has had three neuroleptic trials), in frustration we obtained special permission from Sandoz for her to join a clozapine protocol. Within 3 weeks her florid psychotic symptoms abated, as did her persistent suicidal tendencies and dysphoria. There was no return of tardive dyskinesia, which had resolved when she stopped taking thiothixene. Her global ratings on the Brief Psychiatric Rating Scale (BPRS) had started at 6 (severely mentally ill), went to 5 (moderately severe) within 3 weeks, to 4 (moderate) within 6 weeks, and to 3 (mild) within 20 weeks. She was discharged only 12 weeks after reaching a therapeutic dose (375 mg) of clozapine. After 8 months, she had a score of 1 (no symptoms present) on the BPRS, and currently, after 1 year, she is employed full-time and is seeking independent residence.

In sum, we report a patient for whom clozapine successfully reversed a deteriorating and chronic course. Unlike the typical patient who receives clozapine, ours was not schizophrenic, did not have negative symptoms, and had not failed to benefit from multiple neuroleptic trials. Further, our patient showed continuous improvement over a number of months, suggesting that overall benefits may take some time to manifest themselves.

We welcome this medication's becoming commercially available and advocate its use. We hope systematic studies will observe a broader diagnostic range of patients for whom it is beneficial.

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## An Unusual Case of Capgras' Syndrome

SIR: A large number of case reports of Capgras' syndrome have appeared in the literature since it was first described by Capgras and Reboul-Lachaux in 1923 (1). Association of Capgras' syndrome with certain other interesting psychopathologies, such as the de Clerambault syndrome (2, 3), folie à deux (3), and the Ekbom syndrome (4), has been reported. We report an unusual presentation of Capgras' syndrome, which was accompanied by the de Clerambault syndrome and a peculiar grandiose delusion related to self-identity.

> Ms. A, a 28-year-old woman, presented with a history of suspiciousness, hearing voices, and outbursts of abusive and violent behavior over a period of 10 years. There was also a history suggestive of the de Clerambault syndrome, which involved writing letters to a particular industrialist in which she proposed marriage. Psychiatric examination revealed multiple delusions (including Capgras' delusions) and auditory hallucinations but intact cognitive functions. Results of a physical examination and investigations that included an EEG and a CT scan were normal. A diagnosis of paranoid schizophrenia was made. The Capgras delusions had been continuously present for about a year. The doubles included her husband, her son, other relatives, the therapist, fellow patients not known to her, and strangers. She complained that her son, certain other relatives, and the therapist were impostors posing as her husband. She would not permit her husband to have sex with her, considering it to be incestuous. On seeing fellow female patients or any unknown woman, she would say that they were not women and every one of them was actually her husband. She also revealed that she was not her usual self and had changed into a particular Indian movie star.
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> The patient was given oral trifluoperazine, 20–30 mg/day, and trihexyphenidyl, 4–6 mg/day. Improvement was observed in various psychotic symptoms except the Capgras delusions, which showed no change even after 6 months. Thereafter she was lost to follow-up.

Most of the case reports of Capgras' syndrome refer to delusions of doubles of others. There are only a few reports of patients with delusions of doubles of self (1). Involvement of multiple persons acting as doubles of other persons (i.e., fellow female patients and unknown women) appears to be a unique phenomenon. In addition, the delusion of the son posing as the husband is an unusual phenomenon. The grandiose delusion relating to change of self-identity is also an interesting association.

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## Fluoxetine for the Treatment of Compulsive Facial Picking

SIR: Successful treatment of impulse control disorders and obsessive-compulsive disorders has been reported with various tricyclic antidepressants and, more recently, with fluoxetine (1, 2). Trichotillomania has been a difficult syndrome to treat with behavioral therapy, with traditional psychotherapy, or with medications. A variant of this disorder can be seen in this case of a patient with compulsive picking at facial lesions who left her eyebrows and hair intact.

> Ms. A, a 21-year-old college student, sought treatment for her compulsive need to pick at lesions on her face. She had been unsuccessfully treated for this compulsion since the age of 14. Her symptoms had begun with a relatively mild case of acne, which became seriously compromised by her obsessive picking at rather average lesions. She had consulted a dermatologist, who treated her with antibiotics and local skin therapy. Her dermatologist eventually recognized the self-induced nature of the problem and decided not to use isotretinoin to treat her disorder. She was referred to a psychologist, who evaluated her condition and recommended hypnosis. This was unsuccessful and she returned to her dermatologist, who has followed her case over the last several years.
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> Ms. A's condition progressively deteriorated until she would spend up to 2–3 hours daily picking at her face, unable to restrain herself except for a few days each month. Her skin became markedly inflamed, with many secondary infections, scarring, and general disfigurement. An older brother had shown signs of an obsessive-compulsive disorder that included checking, excessive hand washing, and obsessive slowness. The patient also had many obsessional worries, but her compulsions seemed limited to the aggravation of her facial lesions. No other major psychopathology was demonstrated, and she was successful in a part-time job as well as in her academic performance during her senior year of college.
>
> Ms. A was started on fluoxetine, 20 mg/day; the dose was raised to 40 mg/day after 2 weeks. Within 4 weeks of instituting therapy, she was spending substantially less time picking at her facial lesions. Twelve weeks after she began treatment, her lesions had largely cleared, and she reported only a rare breakdown of her control problem.

This case probably represents a variation of an obsessive-compulsive disorder manifested as an impulse control disorder with self-inflicted facial lesions. What began as a grooming concern deteriorated into compulsive, disfiguring behavior. The biological nature of these disorders is being widely postulated (3), yet conclusive data demonstrating the effectiveness of pharmacotherapy must be drawn from larger samples of such patients, with adequate, double-blind control. This case suggests that the use of appropriate psychotropic medications—in particular, fluoxetine—may offer hope and promise for these patients when other approaches have been less than satisfactory.

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## Fluoxetine for Adolescents With Obsessive-Compulsive Disorder

SIR: Michael A. Jenike, M.D., and associates recently reported the efficacy of fluoxetine in an open trial of adult patients with obsessive-compulsive disorder (1). We have also observed fluoxetine to be useful in treating adolescents with this disorder.

Obsessive-compulsive disorder in adolescents has received much less attention than has the condition in adults, despite recent findings that the disorder is common and debilitating in younger patients (2). In particular, treatment research has lagged. There are only two reported studies of the efficacy of clomipramine in adolescents with obsessive-compulsive disorder; one found it superior to placebo (3), and the other found it superior to desipramine (4). There are, to our knowledge, no reports of fluoxetine being tested in adolescents with obsessive-compulsive disorder.

In open trials, we treated eight adolescents who met the *DSM-III-R* criteria for obsessive-compulsive disorder. All of the patients were between the ages of 12 and 17 years; four were male and four were female. If major depression was present, it was secondary both in onset and in clinical importance. Fluoxetine was generally started at 20 mg/day and raised by 20 mg every 2 weeks to 60–80 mg/day if tolerated and indicated. Concomitant medications were avoided, and 8 weeks was considered a minimum trial before judging efficacy.

To be considered a responder after 8 weeks of treatment, a patient had to demonstrate a reduction of 50% or more in the time spent on obsessions and compulsions and at least a substantial reduction in psychosocial impairment caused by obsessive-compulsive symptoms. Four of the eight patients met these criteria and were considered responders. Two others had more equivocal responses, and the remaining two tolerated the medication poorly and had to stop taking it.

Before treatment the four responders had been highly troubled by washing or other repeating rituals, which largely disappeared by the end of 8 weeks of taking fluoxetine in doses of 20–80 mg/day. The patient who took 20 mg/day was troubled by nausea, which prevented further dose increase; the other responders tolerated the medication well. The two patients with equivocal outcomes tolerated 60 and

80 mg/day well, but showed only modest improvement in obsessive thoughts and checking and in hand washing, respectively. In the latter case only slight further gains were obtained after an additional 4 months of taking 80 mg/day of fluoxetine. The last two patients were so bothered by side effects of jitteriness or headaches and agitation that they could not complete the 8-week trial.

In this small open series, fluoxetine seemed helpful for and well tolerated by half of the adolescents with obsessive-compulsive disorder. The response rate is similar to those reported for clomipramine and fluvoxamine. Controlled trials in larger samples are needed for rigorous testing, however. Further study of fluoxetine in adolescents is urgently needed, since at present it is the only medication with apparent efficacy in obsessive-compulsive disorder that is marketed in the United States. It also has a favorable safety profile; it is not cardiotoxic, has not been associated with seizures when taken in the clinical dose range, and has not been reported as the cause of a fatal overdose except when ingested along with other agents (5).

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## Do Repeated Courses of ECT Cause Brain Damage Detectable by MRI?

SIR: The cognitive impairment after ECT has been attributed to brain damage (1). We read with interest the article by C. Edward Coffey, M.D., and colleagues (2), who found no change in patients' brain structure, as assessed by magnetic resonance imaging (MRI), 2–3 days after a course of ECT. We report a long-term prospective MRI study of a patient who became confused after ECT.

> Ms. A, a 77-year-old woman with well-controlled hypothyroidism, had suffered four previous episodes of unipolar delusional depression despite continuation doses of lithium carbonate. These episodes had responded well to treatment by bilateral ECT. In the summer of 1987 she consented to MRI assessment. She was euthymic on a regimen of amitriptyline, 150 mg/day, and L-thyroxine, 0.1 mg/day, and there was no clinical evidence of dementia. A few weeks later she suffered a recurrence of illness, which was treated by two courses of bilateral ECT (12 treatments in all). The following winter she had a repeat MRI assessment, when she was euthymic and still taking amitriptyline and L-thyroxine. In the spring she suffered a further relapse, and after six bilateral ECTs she became forgetful, confused, and disoriented.
>
> She was reassessed by MRI that summer, when she was cognitively impaired. Her medicine had been changed to lofepramine, 210 mg/day. A 0.08-tesla resistive MRI system was used. The scans were presented in a random order, mixed with scans from other patients, to a certified radiologist (L.W.T.). Spin-lattice ($T_1$) and spin-spin ($T_2$) relaxation times were calculated for each cerebral hemisphere (excluding CSF) from 12-mm-thick transverse sections obtained 10 mm above the widest point of the lateral ventricles, and these were averaged (3). A series of transverse $T_1$-weighted images were obtained at the second and third assessments, which allowed cortical atrophy to be assessed by the method of Skodt et al. (4). The Huckman, ventricular, and cella media indices, which are ratios of brain parenchyma to ventricular space, were calculated.
>
> All the scans revealed minor generalized cerebral atrophy without any abnormality of the brain parenchyma. There was no significant change in $T_1$ relaxation time (368 msec, 374 msec, and 374 msec) or in $T_2$ relaxation time (118 msec, 116 msec, 115 msec) over the year. There was no change in the Huckman (59 versus 50), ventricular (1.21 versus 1.21), or cella media (4.9 versus 5.7) indices to suggest any increase in cerebral atrophy; indeed, the slight increase in the cella media index was in the opposite direction to that expected for progressive cerebral atrophy.

This is the first report of a long-term prospective MRI study of brain structure before and after repeated courses of ECT. MRI scans are never exactly reproducible, as there is always slight variation in the level scanned and in head tilt. However, within these limits, the scans show no support for the hypothesis that the cognitive impairment after ECT is a consequence of brain damage. It may be that ECT does not produce brain damage or that our imaging techniques are not yet sufficiently sensitive to detect it. We hope to report soon on a larger series of patients.

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## Dr. Coffey and Dr. Weiner Reply

SIR: Drs. Scott and Turnbull have provided a useful contribution to the literature with their report that bilateral ECT produced no changes in brain structure or tissue signal, as assessed by MRI, in an elderly woman before and after (at approximately 6 months and at approximately 2 months) she had successive courses of the therapy. Their observations complement our original report, which found no acute changes in brain structure in nine patients assessed by MRI performed 2–3 days after completion of a course of bilateral ECT.

We agree with Drs. Scott and Turnbull about the need for serial follow-up of ECT patients in order to assess the potential for long-term structural brain changes. We are currently conducting such a study, and to date 40 subjects have received brain MRI scans before and after (at 2–3 days and at 6 months) a course of pulse bilateral ECT. A preliminary analysis of our first 30 subjects reveals 1) no evidence of acute or delayed changes in brain structure and 2) no worsening of pre-ECT brain abnormalities, which were surprisingly common in this sample. Additional analyses that use volumetric reconstruction techniques and quantitation of $T_1$ and $T_2$ signal intensities are in progress. We hope to publish these data soon, and we look forward to additional reports from Drs. Scott and Turnbull.

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## Antidepressants and Mania

SIR: I would like to draw your attention to a psychiatric aphorism that illuminates some mood disorder mechanisms: Every antidepressant that does not cure mania *causes* mania. Stated in other words, any antidepressant treatment that is not also efficacious as a mood-stabilizing, antimanic treatment can provoke manic episodes in a patient with bipolar mood disorder.

This principle is well confirmed by the actions of treatments such as tricyclic antidepressants, monoamine oxidase inhibitors, fluoxetine (1), alprazolam (2), and sleep deprivation (3); all of these have been reported to provoke (iatrogenic) mania in bipolar patients. Conversely, lithium, carbamazepine, clonazepam, and valproic acid are effective treatments for mania, and none of these has been reported to cause mania (4).

ECT presents an interesting illustration of the disjunction between mood-elevating and antimanic actions. While it is an effective treatment for both mania and depression, it often induces transient mania. This phenomenon has been noted frequently since Fink and Kahn reported it in 1961 (5), when half of their patients who were given ECT developed manic or hypomanic symptoms. Additional ECTs then resolved this iatrogenic mania and produced a good clinical outcome.

Reports that novel antidepressants fail to provoke mania do not invalidate this aphorism, since these reports are invariably derived from small numbers of patients who are treated in clinical trials before the widespread use of the drugs. The mania-inducing properties of virtually all antidepressant medications were not discovered until after the drugs had been marketed, when the responses of many patients were collated.

The observation that every antidepressant causes mania supports the unidimensional theories suggesting that both mania and depression can be produced by quantitative alterations in the same single chemical process. Clinical variations in the symptom constellation, such as rapid cycling, might be produced by superimposing other treatment-specific effects on top of this basic process.

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## Pyridoxine and Thyroid Function

SIR: Recent studies on thyroid function in patients with premenstrual syndrome (PMS) have detected a large range in the frequency of augmented thyrotropin (TSH) responses to thyrotropin-releasing hormone (TRH) stimulation. At least four studies have been published, and the extremes of augmented responses run from more than 90% of patients (1) to 0% (2). The source of this large range seems to be inexplicable, but reports of the effect of pyridoxine on thyroid function and the TRH stimulation test may clarify this issue. Dakshinamurti et al. (3) found that pyridoxine-deficient young rats developed a hypothyroidism in which their pituitaries were more sensitive to TRH. Study of humans (4) has shown that administration of pyridoxine suppresses the augmented TSH response to TRH in primary hypothyroid patients. Pyridoxine, it seems, can have both a physiological and a pharmacological effect on the pituitary response to TRH.

In the studies of PMS patients, all subjects were "drug free," but none of the studies commented on the patients' dietary habits with respect to their pyridoxine intake or their intake of dietary supplements in general. Pyridoxine and other supplements have become a popular treatment for PMS and can alter its course. It seems possible, then, that all of the authors are correct and that the differences they have found reflect differences in supplement intake by the patients studied.

The implications of this information go beyond just PMS. Augmented TRH test values are present in 10%–15% of depressed patients, and pyridoxine deficiency has been reported in 21% of depressed patients (5). It seems likely that these two groups overlap. If so, should the treatment be thyroid hormone, or is pyridoxine a more fundamental approach, and does the lack of response to thyroid hormone in some depressed patients indicate a need for pyridoxine as well? Or, is the augmented TSH response indicative of another phenomenon and the correction of this responsiveness with thyroid or pyridoxine merely a pharmacological effect without significant alteration of the basic pathophysiology? I suspect that all patient populations are heterogeneous and that several clinical syndromes will be found. Other disorders, such as thyroiditis and altered magnesium metabolism, may be present, making the likelihood of heterogeneity even greater.

Clearly, a more systematic study of the interaction of pyridoxine with altered thyroid function is indicated.

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## Bulimia Associated With Sexual Trauma

SIR: In their extensive review, Alan B. Levy, M.D., and associates (1), investigating possible relationships between bulimia and depression, concluded that bulimia is not a variant of depression. While this conclusion appears reasonable, it provides no guidance for further investigation. Part of the difficulty may lie in their focusing on concurrent depression.

One wishes that the authors had distinguished between bulimia and bulimia associated with anorexia nervosa in their summarization of clinical evidence associating depression with these disorders. The authors quite correctly distinguished the two subsets of eating disorders in reporting the work of others. However, they did not continue this distinction in their own conclusions. It appears that the strongest clinical evidence for concurrent depression cited by Dr. Levy and associates lies in studies reporting bulimia associated with anorexia nervosa.

Our experience with anorexic patients (who may also have concurrent bulimia) suggests a possible avenue for further exploration. Fournier (2) found that women with histories of childhood sexual trauma had psychological profiles similar to those of anorexic patients. Oppenheimer et al. (3) similarly found that 50 of their 78 patients with eating disorders had had adverse sexual experiences (40 of them in childhood). We also have noted an apparently high incidence of convincing histories of early (usually childhood) sexual trauma.

In this group at least, it appears that the outcome is not classical depression but, rather, a typical presentation of the personality structure often associated with posttraumatic stress disorder (PTSD). The presence of intrusive thoughts may be variable, but typically there is a history of repeated abuse, an outcome of avoidance of intimate relationships, and a marked startle response to being unexpectedly touched. The state of dysphoria alternates with, and is temporarily relieved by, the excitation of planning and executing substance-abusing (food) binge behavior. This provides, until the plan is fully executed, a sense of "high" or excited "rush." A guilty, down period then follows, and a subsequent, well-learned cyclic pattern of relief (planning and executing a binge) is repeated. This highly reinforcing pattern has been described in relation to combat-related PTSD (4, 5).

Dr. Levy and associates reported responses to antidepressant medications, a high frequency of suicide attempts, depressionlike symptoms, and a tendency for depression to increase as bulimic behavior decreases. These findings and the lack of correlation with family history of affective disorder are also compatible with our hypothesis.

We cannot yet estimate the frequency with which this cyclic pattern of reinforcement occurs as a subtype of eating disorders. We are certainly impressed that this type of history is commonly associated with binge-purge behavior; it explains some of the treatment-resistant quality of these disorders. The combination of trauma, avoidance of intimacy, and dysphoria relieved by recurring and highly reinforcing, *powerful*, excitatory periods should be addressed. We welcome comment by Dr. Levy and his colleagues and others on their clinical experience in this regard.

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## ECT as Prophylactic Treatment for Bipolar Disorder

SIR: In their excellent review of alternatives to lithium for preventive treatment of bipolar disorder (1), Robert F. Prien, Ph.D., and Alan J. Gelenberg, M.D., omitted mention of the first treatment reported to be effective for this purpose: ECT. In a 1949 article presciently entitled "Prophylactic Electroshock," Geoghegan and Stevenson (2) reported the results of an open clinical trial that showed no relapses over 3 years in 13 manic-depressive patients who received monthly treatments after a course of ECT, compared with frequent relapses in 11 patients who refused such treatment. Two years later, the results were equally encouraging (3).

To my knowledge, no attempt to replicate these results under controlled conditions has been reported. Nonetheless, a 1986 survey of practitioners of ECT (4) found that 59% of the respondents used maintenance ECT (for a median of three patients annually), and I have personally frequently observed the effectiveness of such therapy in carefully selected bipolar patients who continue to relapse despite intensive attempts at pharmacological prophylaxis.

I know that these observations are well-known to Drs. Prien and Gelenberg, whose review was, after all, aimed at pharmacological methods of prophylaxis. But despite the often excellent results obtained with such maintenance drug therapy, there remains a hard core of bipolar patients whose continued residence outside of hospitals seems wholly dependent on maintenance ECT. One can, therefore, heartily agree with Fink (5) that "it is timely to consider this option seriously, and undertake a national effort to assess this form of continuation therapy. Maintenance ECT deserves greater academic and clinical attention."

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### Sleep Disturbance in Posttraumatic Stress Disorder

SIR: In his editorial (1) accompanying our article "Sleep Disturbance as the Hallmark of Posttraumatic Stress Disorder" (2), Charles F. Reynolds III, M.D., offered a thoughtful commentary on our hypothesis that posttraumatic stress disorder (PTSD) may be fundamentally a disorder of REM sleep mechanisms. Citing Cartwright's finding (3) that, among a group of women undergoing divorce, those who were depressed showed a shortened REM sleep latency and a disruption of the normal REM sequence, he appeared to suggest that a "major mood-disturbing event" can disturb dreaming. Consequently, PTSD would not be unique in its association with the repetitive, stereotyped anxiety dream. However, this reasoning does not fully take account of other observations from the same study. "Anxiety dreams" were no more frequent in the depressed women than in a control group of euthymic married women (4). Furthermore, the dreams of the depressed women had a low "dreamlike quality" and *avoided the subject of divorce* (5). They stand in marked contrast to the vivid dreams of PTSD, which often recapitulate the trauma.

Dr. Reynolds emphasized that the depressed women in Cartwright's study, who did not have PTSD, nonetheless had polysomnographic evidence of heightened "REM sleep pressure," which has also been identified in endogenous depression. Thus, if an abbreviated REM sleep latency or an altered REM sequence were to be demonstrated in PTSD, the question of specificity would inevitably be raised. However, while it may not be feasible to control adequately for concurrent depression in PTSD patients (most of whom are or have been depressed), it should be possible to compare the sleep of PTSD subjects and depressed subjects without PTSD. The former group may well display REM sleep patterns that heretofore have not been described in depression. To predict that a particular constellation of REM sleep abnormalities might "mark" PTSD is not to imply that some evidence of REM sleep dysfunction cannot be seen in other psychiatric disorders.

Many of Dr. Reynolds's suggestions for pursuing the hypothesis that aberrant REM sleep mechanisms underlie PTSD fit squarely with our own. It is important to extend questionnaire and sleep diary studies to other patient groups, so that the question of the specificity of the recurrent, stereotyped anxiety dream can be addressed directly. We agree that awakening studies, in which REM sleep and non-REM sleep mentation can be compared in PTSD subjects, are potentially useful. Long-term polysomnographic investigations over the course of treatment might establish correlations between REM sleep measures and dream intensity.

As Dr. Reynolds asserted, the pivotal question is whether the sleep disturbance of PTSD is central to the pathogenesis of this disorder or is an epiphenomenon; experimental strategies using naturalistic and pharmacological probes of the REM sleep system should help to provide an answer. We believe that support for the concept of a core REM sleep dysfunction in PTSD already emerges from the theoretical linkage between REM sleep mechanisms and some of the characteristic waking symptoms of the disorder (1). Thus, investigating the nature of startle and flashback behavior in PTSD, as we have begun to do (6), can provide indirect evidence that ultimately may prove compelling.

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SIR: Some recent observations that I have made on the structure of the manifest dream in troubled patients might shed some light on the problems described by Richard J. Ross, M.D., Ph.D., and associates in their article and by Charles F. Reynolds III, M.D., in his editorial on sleep disturbance in posttraumatic stress disorder. I find that in the dreams of patients with depression, schizophrenia, or borderline personality disorder, one can often identify alternation of two tendencies—one constructive, hopeful, and associated with good feeling, and the other destructive, discouraging, and dysphoric. These two tendencies usually alternate in the dreams of these patients in a full dream sequence that consists of three components. The first is a presentation of the current affective state, the second is a correction characterized by its opposite, and the third is a restatement of the first, as the correction fails. The presenting affective state may be determined by internal dynamic forces or, very often, by the impact of external events.

Every clinician who observes patients in the course of intensive psychotherapy or psychoanalysis will be able to confirm this observation. Let me illustrate with the following dream described by a 45-year-old woman with a cyclothymic character.

> The world was being flooded. The water was reddish and grayish. It was turbulent with white crests. I saw rocks and houses. People were drowning. We were on a high level where there were white houses. I was on a boat, a nice boat, large with lacquered blond wood floors. There was a kitchen on the boat. I became concerned that the boat would capsize. We landed at a house on some land. We brought things onto the boat: glasses—no, plastic cups, for fear that glasses might break—and food.
>
> What's the point of living if you're going to drown? I thought of suicide and became calmer. No, I said, there is always hope. If you die now you eliminate hope.
>
> I saw some people drowning, some with their hands raised, some protesting, some peacefully.

The initial phase of the dream, the flooding of the world, expresses the patient's current depressive affect. The dream then portrays the patient's attempt to save herself and her world by taking refuge on the boat and by landing on high ground, where food became available. Finally, however, suicidal rumination and universal drowning supervene, as the depressive tendency suppresses the attempt at recovery and reasserts itself.

Among depressed patients, the initial and final phases are depressive and destructive, whereas the middle phase attempts some kind of rebirth. Among hypomanic and manic patients, the reverse is true. Among schizophrenic and borderline patients, either sequence prevails, depending on the affect prevailing at the time.

Often, perhaps only two of the three phases are recollected, and sometimes, only one. Which one or which two of the phases of the three-phase sequences are represented can be determined by comparison with other dreams of the same night and by the patient's first waking affect, which generally corresponds to phases 1 and 3. Within this framework, the posttraumatic anxiety dream is obviously phase 1. The patient awakens with anxiety because the corrective phase does not cancel out the initial distress. The reason for this failure of the wish-fulfilling function of the dream is not clear.

Perhaps the manifest dream gives us a window on the unconscious process of affective regulation. However, we cannot rule out the possibility that the dream is itself the process of affective regulation.

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## Differential Diagnosis of Schizophrenia and Multiple Personality Disorder

SIR: In reviewing "Psychotic Disorders in *DSM-III-R*" by Kenneth S. Kendler, M.D., and associates (1), we are reminded of one problem with the *DSM-III-R* criteria for schizophrenia that was not addressed by the authors. Patients with multiple personality disorder commonly hear voices that discuss, argue, direct, or attack, thus leading to inappropriate diagnosis and treatment. This difficulty should be addressed in *DSM-IV.*

In our experience, the voices heard by a patient with multiple personality disorder are reported by her to be originating inside her own head. She may have full, limited, or no insight into the origin of these voices, which are commonly attributed by theorists in the field to dissociated personality states. A patient lacking insight may attribute some of the voices to demonic forces, thus appearing delusional. The most reliable distinguishing feature of the voices in multiple personality disorder seems to be that the clinician can engage the dissociated personality states in conversation; schizophrenic voices are heard only by the patient.

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## Dr. Kendler and Associates Reply

SIR: Drs. Rathbun and Rustagi are correct in stating that the differential diagnosis of schizophrenia and multiple personality disorder was not specifically addressed during the revision of *DSM-III.* It may be, as they suggest, that the ability of the clinician to engage in conversations with the voices is a key to the differential diagnosis. As they are undoubtedly aware, however, there are individuals with classic schizophrenia who claim to be "inhabited" by other beings or personalities.

A generic issue raised by the letter of Drs. Rathbun and Rustagi is the extent to which diagnostic criteria for relatively common disorders should be modified only to address the problems of differential diagnosis with respect to relatively rare disorders. Our own impression is that a textual acknowledgment that multiple personality disorder must be considered in the differential diagnosis of schizophrenialike states would be sufficient for *DSM-IV* and would be preferable to a modification of the schizophrenia criteria themselves.

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## Oxazepam and Carbamazepine for Alcohol Withdrawal

SIR: In reference to the article on oxazepam and carbamazepine in the treatment of alcohol withdrawal (1), Robert Malcolm, M.D., and associates did not state clearly how long the drugs were used, but I infer that subjects were maintained on a fixed dose of a drug for 7 days and then the drug was discontinued. If this is correct, the protocol was not consistent with the typical treatment regimen for alcohol withdrawal; most clinicians prescribe tranquilizers in high doses for 24 hours and then taper rapidly. Given the unique protocol in this study, one cannot conclude that carbamazepine is indeed an alternative to benzodiazepines for routine detoxification.

The authors noted that carbamazepine was more effective than hydroxyzine in decreasing global psychological distress. A previous Veterans Administration study of alcohol withdrawal (2) demonstrated that placebo was more effective than chlordiazepoxide in decreasing psychological distress. The absence of a control group in Dr. Malcolm and associates' study left unanswered the question of what additional benefit carbamazepine provides and its role in the treatment of psychological distress associated with alcohol withdrawal.

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DAVID AMES, M.D.
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### Dr. Malcolm and Associates Reply

SIR: Dr. Ames is correct; we used a 6-hour dosing interval for 7 days for both medications, and then they were discontinued without tapering. Dr. Ames appears to confuse issues of therapeutic efficacy with pharmacokinetic effects. High loading doses of benzodiazepines may be given to withdrawing patients if they are already in delirium or extreme agitation (1). For impending delirium tremens and more moderate cases of withdrawal, patients may be given benzodiazepines or carbamazepine at fixed dosage levels. Tapering of a benzodiazepine is not done to avoid an abstinence syndrome from the benzodiazepine. This would hardly occur in such a short period of use. Benzodiazepines are tapered if their half-lives are long, to avoid accumulation and intoxication. Failure to taper long-half-life drugs could lead to ataxia and dysarthric speech, and the patient would be unable to participate in treatment. A useful feature of both carbamazepine and oxazepam is that they have relatively short half-lives and do not require tapering. We believe our study does demonstrate that carbamazepine and oxazepam are equivalent, both in efficacy and in side effects, for short-term use. We do not claim that carbamazepine should be an alternative to benzodiazepines for routine detoxification. More studies are needed to ascertain whether carbamazepine should replace benzodiazepines for standard-of-care therapy. As we noted, there appear to be indications for preferring carbamazepine over benzodiazepines for certain patients, including those who have had adverse reactions to benzodiazepines, those whose alcohol withdrawal may be complicated by psychiatric illnesses such as bipolar disorder, and those who have had histories of seizures or other severe withdrawal manifestations that did not previously appear to be responsive to benzodiazepines. In our study, there were some psychiatric variables that carbamazepine appeared to improve faster than oxazepam did.

In his second paragraph, Dr. Ames mentions hydroxyzine. We assume he means oxazepam. He cites one study conducted in 1971 which found that placebo was more effective than chlordiazepoxide in decreasing psychological distress. The vast majority of controlled, double-blind trials that have been reviewed since that time do not draw this conclusion. We intentionally did not include a placebo control group for our study because it has been concluded by many investigators that benzodiazepines are more effective than placebo. It has been asserted that it is unsafe and unethical to conduct placebo trials (2) in pharmacologic studies of alcohol withdrawal.

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### Childhood Panic Disorder With Agoraphobia

SIR: James C. Ballenger, M.D., and his associates (1) correctly noted that the investigation of childhood manifestations of panic disorder with agoraphobia is both crucial and largely neglected. The compellingly consistent retrospective evidence of a childhood component of panic disorder with agoraphobia has not been strongly supported by the few existing empirical studies (2). On the other hand, an early clinical report (3) detailing essentially classical panic attacks in young children is now belatedly confirmed, again by clinical observation (1).

I agree that anxiety symptoms in children may be difficult to recognize. First, it is unlikely that anxious children come to clinical attention as frequently as do children with overt behavior disturbances or with depression (which may itself be first evident as a secondary conduct disorder). The discrepancy between affective symptoms reported by children and those symptoms evident to the children's mothers (4) suggests that there might be a similar pattern of parental underrecognition of anxiety symptoms.

Second, the developmentally limited capacity of children to articulate anxiety symptoms, or even to be aware of them as such, may hinder the usefulness of structured interviews in the diagnosis of panic disorder and agoraphobia. I suspect that the "extensive clinical contact" with the children that Dr. Ballenger and associates reported functioned as an instrument with very high specificity and sensitivity, and that the use of a structured diagnostic interview with these children might have been unrevealing, at least at the time of initial clinical contact.

Finally, the discordant cross-sectional and retrospective findings regarding a childhood component of panic disorder with agoraphobia may be quantitative, not qualitative. It is quite possible that most adult recollections of childhood panic disorder and agoraphobia are based on a definite yet subclinical manifestation of the overt disorder. Such a hypothesis is consistent with the suspected genetic contribution to the disorder; the infrequently observed childhood panic disorder with agoraphobia may reflect increased genetic loading and environmental determinants. The subclinical disorder in childhood may very well represent an antecedent to overt illness in young adulthood; current diagnostic instruments would not be useful in delineating such an antecedent.

The investigation of panic disorder with agoraphobia in childhood is long overdue. My own research suggests that the use of an innovative and nondiagnostic system of classification, applied to children at risk for panic disorder with agoraphobia, may be productive. The report of Dr. Ballenger and associates emphasized the need for seriously reevaluating the natural history of the disorder and for avoiding the indiscriminate label of "recall bias" when considering the validity of adults' reports of their childhood experiences.

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## Children With Panic Disorder

SIR: In reference to the recent report by Donna L. Moreau, M.D., and associates on panic disorder in children with family histories of depression (1), we were interested in the finding that symptoms of separation anxiety or depression preceded or accompanied the onset of the disorder. This has not been our experience with six prepubertal children with *DSM-III-R* panic disorder, two of whom have already been reported (2). In our patients, the first panic attack usually preceded the development of separation anxiety or avoidance (typically, school phobia). Our children had family histories of panic disorder rather than depression. Our different experience seems to raise, with respect to children, the issue of prodromal symptoms, whose presence in adult panic patients has been the subject of discussion in this journal (3, 4).

Our second comment concerns the possible association between mitral valve prolapse and panic disorder in children. In our sample of six prepubertal patients, all of whom received echocardiographic examination, we found two cases of mitral valve prolapse. This rate is higher than the prevalence in the general population. We would be interested to know whether other groups studying children with panic disorder have collected data on mitral valve prolapse.

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## Dr. Moreau and Associates Reply

SIR: The letter of Dr. Vitiello and colleagues points most importantly to the need for more systematic clinical study of panic disorder in children. We do not consider our study of six children sufficient to make any generalization. There may very well be a difference between the offspring of parents with panic disorder and those of parents with major depression. We are just completing an assessment of approximately 100 offspring of parents with panic disorder, major depression, or both and will have data on the course of illness. We are pleased to see that clinical studies are following up the observation, based on the Epidemiologic Catchment Area study, first made by Von Korff et al. in 1985 (1), that a large number of adults with panic disorder retrospectively reported that the first onset of their disorder occurred in adolescence or even before. Clearly, direct study of children is called for.

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## Biases in Family Assessments of Depression in Patients With Alzheimer's Disease

SIR: The recent article by Thomas B. Mackenzie, M.D., and associates (1) raised important questions about the collection and integration of family data in assessing depression in patients with Alzheimer's disease. Using a standardized interview, they found that "the rate of depression rose nearly fourfold (from 13.9% to 50.0%) if diagnosis based on data from the patient interview was replaced with diagnosis based on information supplied by the family" (p. 1177).

The areas of greatest divergence between ratings by family members and direct patient ratings were in the reporting of symptoms such as loss of interest, irritability, being overly tired, etc. The family members generally reported more symptoms than the patients, and the authors suggested that this reflects the difficulty family members have in "assigning etiological status to symptoms common to depression and dementia" (p. 1177).

An important alternative or additional explanation for these findings which was not explored by the authors is that family members of Alzheimer patients are themselves depressed, and as a result their ratings of others are negatively biased. Support for this explanation comes from several sources. First, the literature indicates that caregivers of Alzheimer patients have high rates of depression (2, 3). Second, individuals with high levels of depressive symptoms are more likely to rate others, particularly individuals they are close to, as similarly depressed (4, 5). Third, these ratings may bear little relationship to the objective status of the person being evaluated. For example, Schulz and Decker (5) carried out a study in which elderly persons with spinal cord injuries were asked to complete the Center for Epidemiologic Studies Depression Inventory. Caregivers of these patients were asked to complete the same scale for themselves and for the patients. The resulting pattern of correlations was very consistent with the point we are making. The relationship between the caregiver's self-rating and the caregiver's rating of the patient was highly positive (r=0.70); however, the relationship between the patient's self-rating and the caregiver's rating of the patient was essentially zero (r=0.02). Individuals who are themselves distressed tend to see those close to them in a similar light.

This explanation is not meant as a substitute for the one offered by Dr. Mackenzie and associates but is presented as an additional alternative worthy of exploration. If data on depression in the family members of the Alzheimer patients are available, it would be relatively easy to test this alternative explanation. We would predict that 1) the disparity in rates of depression is at least in part attributable to negative affect or depression among the caregivers and 2) that there is a concordance between the depressive symptoms of the caregivers and the patients.

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## Dr. Mackenzie and Associates Reply

SIR: In a population of patients with probable dementia of the Alzheimer type, we observed a significant difference in the prevalence of depression depending on whether the information base was provided by the patient or the family. The magnitude of this difference was nearly fourfold. In trying to identify variables that were correlated with diagnostic disagreement between family and patient in which the former endorsed depression and the latter did not, we reported on two variables related to the mood state of the family members. First, they completed the Beck Depression Inventory. As presented in table 1 of the article, there was no significant difference (t=1.38, df=28, p=0.18) in mean Beck inventory scores between family members who endorsed depression in the patient (7.1) and those who did not (4.9). The means of both groups were below 10, the scoring threshold for mild depression. We cannot exclude a type II error due to sample size.

A second way of looking for a negative bias in the family members was to ask them how they would feel "in the patient's shoes" (see table 1). Here, the difference between the mean scores of the concordant and discordant groups was small and insignificant (5.5 versus 6.1; t=1.05, df=29, p=0.30).

On discriminant analysis (not reported in the article), two variables, family rater's certainty about the patient's mood and previous history of treatment for a mental disorder, grouped 81% of the cases correctly. Variables regarding the family member's mood state did not contribute to the accuracy of the case assignment.

Drs. Schulz and Williamson are certainly correct in observing that a family member's mood may negatively affect his or her report on critical diagnostic points, especially those related to mood state. However, statistical analysis of our data did not support mood state of the family rater as a powerful determinant of the observed diagnostic disagreement.

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## Late Luteal Phase Dysphoric Disorder and *DSM-III-R*

SIR: One must credit Robert L. Spitzer, M.D., and associates for their bold effort in defense of including late luteal phase dysphoric disorder as a *DSM-III-R* psychiatric disorder (1), adding to the burgeoning accumulation of variations of human emotion labeled as mental illnesses. My objection to the labeling of this disorder as a mental illness is not an ideological issue, as is the case for those who fear loss of insurance coverage if premenstrual syndrome (PMS) is reclassified as a type of mental disorder. I take issue with Dr. Spitzer and colleagues on, I believe, solid scientific territory, namely, that late luteal phase dysphoric disorder—a condition whose etiology is (by their own admission) unknown—is assumed to be exclusively associated with ovular menstrual cycling. How will Dr. Spitzer and colleagues classify premenstrual dysphoria in the millions of women who use ovulation-suppressing contraceptive pills and others who periodically, and by no means infrequently, have physiological anovular cycles? The follicular phases of these menstrual cycles do not metamorphose into corpora lutea! In addition, anovular menstrual cycles are usually painless (2), and therefore premenstrual dysphoria without physical discomfort (a criterion used by Dr. Spitzer and colleagues in differentiating late luteal phase dysphoric disorder from PMS) is more likely to occur in women lacking a late luteal phase of the menstrual cycle.

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Medical Diagnosis and Treatment. Los Altos, Calif, Lange Medical Publications, 1977, p 422

THEODORE PEARLMAN, M.D.
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## Dr. Spitzer and Dr. Severino Reply

SIR: It is not clear to us whether Dr. Pearlman is merely taking issue with the use of the term "luteal phase" in late luteal phase dysphoric disorder or whether he believes that the condition is merely one of the "variations of human emotion" and therefore should not be classified as a mental illness. He does raise interesting issues regarding the centrality of luteal functioning in the disturbance.

The diagnosis of late luteal phase dysphoric disorder assumes that women with the disorder have, for reasons that are not yet clear, mood disturbance which is associated with the late luteal phase of the menstrual cycle. The fact that many women with this disturbance obtain relief from their symptoms with surgical or pharmacologically induced ovariectomy, which eliminates the luteal phase (1, 2), supports this assumption. A comprehensive review of the effects on premenstrual symptoms of ovarian suppression has recently been published (3).

Dr. Pearlman asks us how we would classify premenstrual dysphoria in women who, for whatever reason, are having physiological anovular cycles; that is, there is no luteal phase. First of all, we know of no data that indicate how common such a condition is, and we suspect that it is relatively rare compared to late luteal phase dysphoric disorder. However, the existence of such a condition (which, by definition, is not late luteal phase dysphoric disorder) does not invalidate the concept of late luteal phase dysphoric disorder.

As we explained in our article, one of the reasons that we used the term "late luteal phase" rather than "premenstrual" is the well-known fact that many women with the disturbance continue to have symptoms even after a simple hysterectomy has stopped menstruation (4, 5). Thus, it seemed that the former term was more accurate (despite its clumsiness) than the latter.

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## Duty to Protect and Gun Control

SIR: The editorial by Pierre Gagné, M.D. (1) commenting on the article by Paul S. Appelbaum, M.D., and colleagues (2) provided a thought-provoking view of why psychiatrists should carefully consider attempts to limit liability through duty-to-protect legislation. As a member of APA's Council on Psychiatry and Law, I fully supported the position advocated by the Appelbaum et al. article. However, recent experience in Oregon makes me seriously reconsider this view.

Issues related to the *Tarasoff* doctrine are ubiquitous, whether they are related to unidentified possible victims, property, motor vehicle drivers, or human immunodeficiency virus infection. The *Tarasoff* dream—that risk can be accurately assessed and that harm can be prevented—is overwhelmingly appealing to public policy makers.

In Stockton, Calif., on Jan. 17, 1989, a man used a semiautomatic AK-47 rifle to kill five children and wound 30 others. This tragic event brought with it a significant resurgence of interest in gun control. The California legislature passed a bill limiting the purchase of attack weapons. On the federal level, President Bush limited imports of these weapons.

The Oregon legislature's approach was to move to tighten gun purchase requirements and expand the list of persons prohibited from acquiring handguns. An alliance was forged between the National Rifle Association, law enforcement groups, and those with long-term interests in gun control to put together a bill that would keep guns out of the hands of the "unfit," including the mentally unfit. The gun bill was described by one of its legislative sponsors as "nut control rather than gun control."

A key provision of the gun control bill was linked to reporting requirements under another proposed bill, a duty-to-protect proposal similar to the APA model statute. Any person reported to the police under the duty-to-protect bill would in turn be automatically reported to the State Health Department, which would maintain a registry of these "dangerous" persons. This list would be available for police review when an individual attempted to purchase a gun. An individual could appeal the appearance of his/her name on this list. Without a successful appeal a person's name would remain on the list for 4 years.

Our district branch, which had originally cosponsored the duty-to-protect bill, withdrew its support from this bill. We took the position that the potential for abuse of reporting under the gun bill and the negative and unacceptable effect on mental health care of the development of a registry of dangerous persons far outweighed our need for the duty-to-protect legislation. Fortunately, in the 11th hour of the legislature session, the duty-to-protect bill failed to emerge from conference committee, resulting in the deletion of the registry provisions of the gun bill. The gun bill did become law.

I write to alert readers to this potential, new linking of duty-to-protect legislation and gun control or similar measures involving the identification of dangerous persons. I personally would not support the introduction of a duty-to-protect bill again. We would be better off taking our chances in the courtroom than accepting the risk of misuse inherent in the development of a registry of dangerous persons. Dr. Gagné's cautions, although not the same as those described in this letter, are significantly more meaningful to me now than they would have been 6 months ago.

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### Dr. Appelbaum and Associates Reply

SIR: Although the events reported from Oregon by Dr. Bloom are disturbing, we disagree with his conclusion that they should lead to a rejection of all efforts to limit psychiatrists' duty to protect third parties. Legislation restricting the duty has not, to our knowledge, resulted in attempts to misuse information generated in psychiatrists' reports in any of the 15 states that have adopted such laws.

Nor is duty-to-protect legislation the only, or even the most likely, means by which a legislature bent on avoiding dealing with gun control or other major issues can abuse the rights of the mentally ill. Had the Oregon legislature been so inclined, it could have required that all reports made under existing law (psychiatrists in Oregon have a common-law duty to protect third parties [1]) be entered in a registry, or that all patients about to be released from psychiatric facilities be evaluated for capacity to own a gun, with conclusions reported to the state. Registries of "dangerous" persons already exist to some extent. The U.S. Secret Service, for example, maintains a list of people, many of them mentally ill, who have threatened the life of the President. Abandoning legislation restricting the duty to protect will not prevent the development of such registries—appropriate or not—in the future.

There may, however, be a lesson to be learned from the Oregon experience. Psychiatrists concerned about the possible misuse of reports made to police might consider supporting duty-to-protect legislation that imposes restrictions on the use of information obtained from therapists. For example, in addition to use of the information to protect potential victims identified in therapists' reports, use might be limited to criminal prosecution or defense related to patients' violence. That should preclude the ill effects feared by Dr. Bloom without negating the beneficial impact of limiting psychiatrists' liability.

REFERENCE

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### Comments on Review of Book on ECT

SIR: Dr. Brian J. Masterson's otherwise extremely generous comments on my recent textbook on ECT (1) included a few asides that may puzzle *Journal* readers as much as they puzzled me and that deserve comment. 1) The year 1965 was not "the year a new age of ECT began with the use of modern anesthetic agents"; this occurred a decade earlier. 2) I simply do not find either a "defensive nature and tone" to the volume or any "awkward footnoting in the body of the text." (Indeed, the book contains no footnotes.) 3) Unlike most patients and their families, as well as hospital staff members, Dr. Masterson seems nonchalant about the cognitive side effects of ECT and what he describes as "our society's valuation of memory." I do not agree that one chapter on the subject out of 11 constitutes a "disproportionate amount of space" devoted to the topic. 4) His stress on the importance of training in advanced cardiac life support for doctors who give ECT is idiosyncratic and may reflect local practice at his institution, where, I am given to understand, ECT and ECT anesthesia are administered by residents working alone.

More important, the declaration that I stress "only unilateral treatment" will be more than puzzling to anyone familiar with my work, since for the past decade I have been virtually alone in arguing for the therapeutic superiority of bilateral over unilateral ECT—so much so, in fact, that Dr. Masterson's comment that "some professionals and institutions prefer and use bilateral ECT almost exclusively" might well refer to me! The chapter devoted to unilateral ECT examines in detail each of the nine controlled comparisons—including two of my own—that demonstrate a therapeutic advantage of bilateral ECT. Although I conclude with the recommendation that unilateral ECT, with its relative paucity of cognitive side effects, be given an initial trial in every patient, I specifically *exclude* agitated, delusional, or suicidal melancholic patients, acutely manic patients, catatonic patients, and high-risk, medically ill patients—that is, almost all seriously ill patients—and further advise switching to bilateral ECT in the remaining patients if four to six unilateral ECTs have not done the job.

REFERENCE

1. Masterson BJ: Book review, R Abrams: Electroconvulsive Therapy. Am J Psychiatry 1989; 146:1220–1221

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### An Occupational Hazard of Psychiatrists

SIR: I am moved to record an occupational hazard of psychiatrists apart from the assumed higher incidence of psychopathology and assault by patients. As a right-handed neurobehaviorist in my early thirties, I assume a different attitude (and posture) during psychotherapy sessions than I do during consultations in my specialty, which I approach with zest. Recently, over a period of weeks, I noticed paresthesias and mild sensory loss on the dorsal and palmar surfaces of the fifth finger and medial half of the fourth finger, as well as a zone extending to the wrist, of my left hand. This sensory change coincided with my finally bringing a new, more comfortable chair out of the hospital to use during psychotherapy sessions. I soon realized that it would worsen as I leaned with my left elbow on the armrest, either with a shift of my weight to that side or with increased flexion at the joint and the added pressure of my head; relief was obtained by allowing the arm to dangle straight down.

The ulnar nerve can become compressed at the elbow in the cubital tunnel, with additional narrowing occurring during flexion. Nerve entrapment from thickening of the aponeurotic arch between the two heads of the flexor carpi ulnaris or bulging of the medial collateral ligament of the elbow joint can produce the cubital tunnel syndrome, including, in its full form, the sensory changes I have described, a "claw hand" deformity, and paresis of ulnar flexion. One should be on guard against prolonged postures of any sort because of the possibilities of pressure neuropathies; I guess this one could be called "pseudotherapist's elbow."

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*Reprints of letters to the Editor are not available.*

# APA Council Reports

*At the fall component meetings of the American Psychiatric Association in Washington, D.C., on Sept. 12–16, 1989, the APA councils heard reports from their components. Following are summaries of the activities of the councils and their components.*

## The Council on Aging

Jerome Albert Yesavage, M.D., Chairperson

With this report, the Council on Aging marks the beginning of its second decade of operation. The hallmark of the new decade is surely the approval by the American Board of Psychiatry and Neurology and the American Board of Medical Specialties of the certificate of added qualifications in geriatric psychiatry. With the first board examination, which is expected to occur in 1991, an additional cadre of geriatric psychiatrists will emerge. The council's members have continued to play an important role in defining the physician-psychiatrist's leadership in diagnosis of and provision of care to elderly individuals with mental disorders.

During the past year, the council has collaborated extensively with other APA components and offices and with other medical organizations. The council continues to be proud of its work with the APA Division of Government Relations, the National Institute of Mental Health, and the National Institute on Aging (the deputy director of which is a former council chairperson). As the council has grown, its advice and consultation have been sought by an ever-widening circle of organizations and individuals; council members have been asked to participate in conferences of other organizations, at Congressional hearings, and in other forums to raise awareness and to promote broader understanding of the needs of the mentally ill elderly. Council members have prepared a list of areas of expertise for Congressional and executive branch testimony. The council has continued its active liaison with the American Association for Geriatric Psychiatry, the National Voluntary Organization for Independent Living for the Aged (part of the National Council on Aging), the American Association of Retired Persons, and the International Psychogeriatric Association. Further, we look forward to continued involvement in the activities of the American Geriatrics Society and the Gerontological Society.

The council's work in 1989 included the publication of a book, a task force report, and its first *Psychiatric News* article. The layperson's *Over 50 Guide to Psychotropic Medications* was published by the American Psychiatric Press, Inc., by the time of the annual meeting. The Division of Government Relations has sent copies of this book to members of Congress and to other associations. The task force report *Nursing Homes and the Mentally Ill Elderly* was published in September 1989: two copies have been sent gratis to each district branch, and the Division of Government Relations has sent a copy to Congress.

A designated work group of the council is working with the Committee on Women to develop a presentation for the 1990 APA annual meeting on issues related to mental health and mental illness in aging women. Yet another work group is considering the scope and content of a charge to a new component that will focus on patterns and modes of services delivered to the mentally ill elderly. This work group may be incorporated into a new committee on long-term care, services, and treatment for the elderly.

The *Task Force on Reimbursement Options and Alternatives in the Psychiatric Care of Older Persons*, Howard H. Goldman, M.D., chairperson, has undertaken a number of activities. The task force members are contemplating developing a brochure for patients that would detail coverage for psychiatric care under Medicare. Dr. Goldman is also serving as vice-chairperson of the APA Council on Economic Affairs, thus forging an important link with other APA components.

The *Task Force on Ethnic Minority Elderly*, Kenneth Sakauye, M.D, chairperson, has drafted its report on minority elderly who need psychiatric care. This extensive review of available literature and statistics will be submitted to the council by January of 1990.

The *Task Force on Education and Training in Geriatric Psychiatry*, Charles Shamoian, M.D., chairperson, is developing a report that will differentiate the content of general psychiatry residency training from fellowship training in geriatrics, continuing medical education in geriatric psychiatry, and fellowship programs. The task force plans to have its report ready by the annual meeting in 1990 and has established liaison with the Council on Medical Education and Career Development.

The *Task Force on the White House Conference on Aging*, Sanford I. Finkel, M.D., chairperson, held its second meeting at the 1989 annual meeting. The task force is postponing additional meetings and document preparation until the White House Conference on Aging has officially been called by the President.

The *Corresponding Task Force on Geriatric Psychiatry in the Public Mental Health Sector*, Barry Fogel, M.D., chairperson, has drafted a paper and will rewrite it for circulation to the council. Operating with minimal APA funding, the task force members have conducted business by means of conference calls.

After approval by the Joint Reference Committee, APA's Board of Trustees established the Task Force on Models of Practice in Geropsychiatry. This task force will be appointed by 1990 and will produce a resource document for physicians contemplating a career in geropsychiatry and for those currently in the field.

Finally, recognizing the importance of the Council on Aging, APA appointed two staff people to work with the council, Ellen Smith as staff liaison and Anita Porter as staff assistant.

# The Council on Children, Adolescents, and Their Families

Lawrence A. Stone, Chairperson

Again, this past year the council has directed multiple efforts toward informing the APA membership (through symposia, written reports of studies, and liaison activities) of matters that specifically relate to children, adolescents, and their families and are of concern to the APA general membership. The purpose of the council—to maximize the effectiveness of APA in addressing the mental health needs of children, adolescents, and their families—has been highlighted during each of these efforts.

Several changes in membership and leadership took place in 1989. Dr. Lawrence Stone was appointed chairperson, and Dr. John Looney succeeded Dr. Stone as vice-chairperson. Dr. Cynthia Barnes joined the council as observer-consultant. Dr. Richard Athey, APA/Burroughs Wellcome Fellow, and Dr. Alice Mao, APA/NIMH Fellow, also joined the council.

The Committee on Juvenile Justice Issues, the Committee on Family Violence and Sexual Abuse, the Committee on Psychiatry and Mental Health in the Schools, the Committee on Chronically Ill and Emotionally Handicapped Children, and the Task Force on Psychiatric Aspects of New Reproductive Technologies made significant presentations during the annual meeting. Each session was well attended and was determined to be a successful educational endeavor. Each component has submitted an abstract for a presentation at the 1990 annual meeting.

The *Committee on Psychiatry and Mental Health in the Schools*, Irving Berkovitz, M.D., chairperson, continued work related to the development of a monograph, "Psychiatric Consultation in Schools." It is anticipated that the final draft will be submitted to the council early in 1990. Several efforts have been directed toward identifying child psychiatrists who work as school consultants and establishing an effective communication system that will allow for the collection of pertinent data. Contacts have been made with more than 100 psychiatrists who have been identified as school consultants. An article describing the work of the committee was published in *Psychiatric News* and should generate additional responses from the membership. The topic of the 1990 annual meeting workshop is "School Programs to Reduce the Effects of Violence."

Members of the *Committee on Juvenile Justice Issues*, William Buzogany, M.D., chairperson, conferred with the primary reviewers (for the Joint Reference Committee) of the monograph "Psychiatrists and the Juvenile Justice System" about recommendations for revision. The committee has begun the rewriting, using the input of the reviewers and a guest consultant. "Capital Crimes and Capital Punishment in Minors" is the theme of their symposium planned for the 1990 annual meeting. The committee plans to develop a position paper on the violent adolescent. The paper will address screening, assessment, full evaluation, treatment (when indicated), public response to adolescent violence, the psychiatrist's role at disposition, a system of diversion from corrections, diagnostic categories, and problems with the conduct disorder diagnosis. In response to separate requests from its parent council and the Council on Psychiatry and Law, the committee is working on a position paper on the psychiatric hospitalization of youth for inappropriate reasons (i.e., behaviors alone) and inappropriate hospitalization for substance abuse.

The *Committee on Family Violence and Sexual Abuse*, Sandra Kaplan, M.D., chairperson, has continued to make progress on the book *Family Violence: A Clinical Guide*, which will be published by the American Psychiatric Press, Inc. (APPI). The volume will consist of chapters covering the following types of maltreatment: spouse abuse, elder abuse, physical abuse of children, sexual abuse of children, child neglect (including emotional maltreatment), and adult psychiatric patient and family maltreatment. The council is responsible for reviewing all drafts before submission to APPI. The committee met with a representative of the National Alliance for the Mentally Ill and Dr. Mary Jane England (representing the Robert Wood Johnson Foundation) to obtain pertinent information. The committee completed a position statement on child neglect and abuse; the statement is to be reviewed by the council before it is referred for adoption and publication.

The *Committee on Chronically Ill and Emotionally Handicapped Children*, Cynthia Pfeffer, M.D., chairperson, met with a representative from the National Alliance for the Mentally Ill to exchange information on chronically ill children and adolescents and their families. The committee has written abstracts for presentations at the 1990 annual meeting on chronic factors associated with vulnerability to conduct disorders, diagnostic stability in conduct disorders, and double diagnoses of mental retardation and psychiatric disorders.

The *Task Force on Psychiatric Aspects of New Reproductive Technologies*, Miriam Rosenthal, M.D., chairperson, continued to gather data from consultants and from clinical material provided by the members. Issues involving the effects of reproductive technologies on children have been addressed by consultants. The need for greater involvement of psychiatrists in addressing intrapsychic features has been emphasized. A workshop is planned for the 1990 annual meeting.

The *Work Group to Develop a Handbook for Psychiatric Practice Related to the Juvenile Justice System*, Michael Kalogerakis, M.D., chairperson, is funded by a grant from the Kenworthy-Swift Foundation. Plans call for a request for new funding, which would allow completion of the work within a year. This component has also submitted an abstract for a presentation at the 1990 annual meeting.

The council identified a number of important issues, for which there were in-depth discussions and/or plans for further study. Dr. David Pruitt provided the council with an extensive report (including history, current programs, and unmet needs) on child care initiatives. An action item—a component to study day care of preschool children—was generated. Dr. Irving Phillips, liaison appointee to the Task Force on the Homeless Mentally Ill, reported on the work and plans of that group.

Another topic addressed was the planned closing of inpatient psychiatric facilities for children and adolescents in some states. The council plans to confer with other components to determine means of maintaining these necessary services.

Liaison activities have continued to be a significant aspect of the council's work. Drs. Lawrence Hartmann and Cynthia Rose, representing the Board of Trustees and the Assembly, respectively, have continued to work with and for the council. Dr. Michael Fishman has kept the council abreast of government programs pertaining to children and adolescents. The annual Caucus of Child and Adolescent Psychiatrists, which meets during the fall committee meetings, is another avenue for exchange of information that pertains to children and adolescents.

# The Council on Economic Affairs

Robert Gibson, M.D., Chairperson

The work of this council and its components during 1989 reflects an ever-increasing effort by psychiatry to influence expanding governmental and commercial interests in the health care field. The council continues to foster nondiscriminatory mental health insurance coverage, to collaborate with other APA components involved in educational programs for purchasers of health insurance, to articulate and promote fair and adequate standards of practice, to oversee the development and refinement of quality assurance programs, and to identify needs and resources for data related to these tasks.

In addition to the assistance provided by the Office of Psychiatric Services, the council and its components look to the Office of Economic Affairs for major technical support of their activities. The Office of Economic Affairs is engaged in a number of efforts, including gathering and disseminating information, creating and maintaining specialized data bases, research, and special projects for various committees and task forces. It also provides technical assistance, such as helping members deal with issues regarding alternative delivery systems. *Ecofacts*, the quarterly newsletter produced by the office, continues to meet with resounding success in its second year of publication.

The attention of the *Committee on Quality Assurance*, George Wilson, M.D., chairperson, was absorbed over the past year by the changing conditions for APA participation in quality assurance review programs. Under APA, CHAMPUS utilization management had evolved through several phases, and CHAMPUS became interested in developing a national telephone-based preauthorization review system. A request for proposals for such a contract, encompassing the largest single review program in the nation, was circulated early in the year. The bidding was highly competitive. APA's Office of Quality Assurance contracted with a health care consulting firm to prepare APA's proposal. Throughout the year, the Board of Trustees discussed the implications of both receiving and not receiving the award. If APA received the award, its Office of Quality Assurance would have to triple in size and begin new operations in an extremely brief time. The potential expansion raised momentous legal, fiscal, administrative, and structural questions. On the other hand, the loss of the award would result in significant financial losses and the need to reduce or terminate other existing quality assurance review programs.

On Sept. 23, 1989, after the fall component meetings, APA learned that CHAMPUS had awarded its large contract to another Washington-based bidder. Subsequent APA decisions to withdraw from active review programs were largely based on the costs associated with operating them, which the association could not support without several large ongoing contracts or a single large contract, such as CHAMPUS. Although the review programs ended on Dec. 31, 1989, APA will continue to be active in the area of quality assurance policies and standards; specific directions and functions will be decided over the next several months. While considering an effective role for APA, the committee continues work on a modified version of the *Manual on Psychiatric Peer Review*. With encouragement from the Assembly, the committee also has discussed ways in which APA might develop standards for review organizations and might participate in the development of practice guidelines.

The *Committee on Hospital-Based or Hospital Related Services*, Boris Astrachan, M.D., chairperson, focused on a proposal by the Joint Commission on Accreditation of Healthcare Organizations (JCAHO) to return state hospitals to accreditation survey under the *Consolidated Standards Manual*. APA has supported surveys of state hospitals under the *Accreditation Manual for Hospitals* for several years. The latter focuses on hospitals and gives greater emphasis to medical leadership. The *Consolidated Standards Manual* gives attention to psychiatric facilities but does not call for medical leadership. On the committee's recommendation, the APA Board of Trustees reaffirmed certain principles on which it has based its proposals to the JCAHO, including the following.

1. Like facilities should be surveyed with like standards. Hospital-based standards should be used for psychiatric units in general hospitals and psychiatric hospitals.
2. Standards must be appropriate to the services being reviewed. (There is a pressing need to develop adequate standards for review of ambulatory and residential care, psychosocial rehabilitation services, psychiatric services in managed care settings, etc.)
3. Medical oversight of medical practice is basic to high-quality care.
4. The medical staff organization is a vital component of hospital organization.
5. APA remains deeply concerned with improving standards of practice in state hospitals. Standards must address the specific needs of those facilitites, including oversight of their rehabilitative activities and links between hospital and community services.
6. Adequate numbers of well-trained surveyors are needed for appropriate review of psychiatric hospitals, units, and services.

At the same time, the Board reaffirmed its ongoing commitment to state hospital systems and to the Association's continued involvement in activities that support public sector practice. Partly in response to APA's concerns, the JCAHO formed a task force consisting of representatives from both the Hospital Accreditation Program Advisory Committee and the Psychiatric Facilities Advisory Committee. The task force was charged with returning to those committees recommendations for short-term and long-term solutions. APA believes that the status quo in state hospital accreditation is not adequate but that a reversion to the consolidated standards would be regressive.

The *Committee on Interprofessional Affairs*, William Webb, M.D., chairperson, continues its work with the Joint Commission on Interprofessional Affairs. The commission is made up of representatives from APA, the American Psychological Association, the National Association of Social Workers, and the American Nurses' Association. Originally formed in 1974, it was envisioned as a mechanism by which these professions could resolve differences and identify areas of collaboration. The Joint Commission on Interprofessional Affairs has published several joint documents and statements, an annual leadership conference involving several elected officers and the chief executive officer of each group has been established, and the chief executive officers of the four organizations now meet regularly. The current tension among the professions has raised questions about the usefulness of continuing this forum, but the value of maintaining an open channel of communication between the four core mental health professions was reaffirmed by the council. The commission continues to provide a means for highly useful informal contact and dialogue between the leaders of the professions. During the course of the year, the APA Committee on Interprofessional Affairs encouraged the areas and district branches to establish mechanisms for discussion with other mental health professions at the local level, if appropriate, using the model of the Joint Commission on Interprofessional Affairs.

The *Committee on Financing and Marketing*, Robert O. Friedel, M.D., chairperson, continued to pursue definitions and strategies to help "customers" define their needs more explicitly and to identify how APA might best assist with meeting those needs. The committee focused on 1) high-quality, cost-effective care, 2) mental disorders as diseases rather than self-inflicted behavioral weaknesses, 3) increased access to care, 4) parity of coverage, and 5) the perceived role of psychiatrists in the mental health care system.

In conjunction with the Office of Economic Affairs, the committee developed a marketing manual intended for use by the district branches. Additional attention in the coming year may be given to 1) media representation of the role of psychiatrists in the mental health care system, 2) external utilization review companies, especially those in managed care systems, and 3) parity of coverage.

The *Task Force on Future Trends in Private Insurance*, Gary Tischler, M.D., chairperson, focused its efforts on documenting APA positions. Utilization management is a key issue being explored by the task force, which is interested in its impact on clinical care, especially given the perception of some policy makers that utilization management is tantamount to clinical intervention. The committee made several recommendations for APA consideration, including the recommendations that APA assume a greater leadership role in influencing state regulation of utilization review and case management activities and that APA be more actively involved in development of guidelines for managed care systems and of minimum criteria for quality review within an organization.

This task force also supported increased efforts by APA to monitor the potential for a national health plan. The council concluded that APA's Division of Government Relations and various APA components are currently monitoring government policy, including aspects that would have to be incorporated in any proposal for a national health insurance plan.

The *Task Force on Psychiatrist Payment*, Boris Astrachan, M.D., chairperson, was established to examine the nature of psychiatrists' income, including the diversity of practice settings, sources of reimbursement, costs associated with various types of practice, the impact of public and private coverage, and the ramifications of changes in health care organization. The task force continues to develop a series of papers on various economic aspects of psychiatric practice.

The *Task Force on Prospective Payment Issues*, Joseph T. English, M.D., chairperson, continued to monitor payment issues and to explore potential alternative payment mechanisms. Among these efforts was a review of studies by the National Institute of Mental Health (NIMH) and of federal legislative and administrative activities related to prospective payment for psychiatry. The task force believes there are no immediate threats to psychiatry's exempt status within the prospective payment system but cautioned the council about an emerging perception in the field that the recent increase in psychiatric facilities may be related to the exempt status. Several initiatives are under way in the states to develop systems for psychiatry involving modifications of diagnosis-related groups; these are being watched closely by the federal government and the field.

The *Task Force on Social Security Income/Social Security Disability Insurance*, Arthur T. Meyerson, M.D., chairperson, remained active. In September it reviewed the Social Security Administration listings for mental impairment for children. Working with the APA Division of Government Relations, the task force ensured APA input in the decision-making process. The task force, in conjunction with the Social Security Administration and the APA Office of Psychiatric Services, again offered its seminar on disability evaluation at the APA annual meeting. A presentation is also scheduled for the 1990 meeting in New York.

The *Work Group on the Harvard Resource-Based Relative Value Scale Study*, Donald Scherl, M.D., chairperson, was formed in June 1988 by the Board of Trustees to monitor new federal proposals for paying physicians under Medicare and to develop positions for the Board. The work group hired consultants to evaluate the original Harvard report on a resource-based relative value scale (RBRVS) for psychiatry and detailed for NIMH, the Congressionally mandated Physician Payment Review Commission, and Congress the problems with the report's section on psychiatry. Testimony provided to both the Physician Payment Review Commission and Congress resulted in the funding by NIMH of a "refinement of the psychiatry RBRVS." Further activities for the work group include identifying areas of potential change in the resurvey for psychiatry, developing substantive data with which to evaluate payment reform proposals currently before Congress, and informing and updating the APA membership about potential changes in physician payment.

In June 1989, on the recommendation of the Assembly and several councils, the Board of Trustees established the Committee on Managed Care under the auspices of this council. The task force is charged with developing a definition of managed care and organizing priorities and draft positions regarding the provision of psychiatric care and the role of psychiatrists in managed care settings. The council noted that some people use the term "managed care" to describe certain delivery systems, such as health maintenance organizations or preferred provider organizations. Others use the term to mean utilization and case management activities. In connection with this task force, "managed care" largely refers to the former.

The *Committee on Occupational Psychiatry*, Peter L. Brill, M.D., chairperson, was under the Council on National Affairs for several years. Recognizing that this committee addresses problems of large corporations concerned about mental health benefits, as well as treatment, for their employees, this committee was reassigned in the last year to the Council on Economic Affairs. The committee has sponsored several special meetings between APA leaders and corporate representatives, is considering a curriculum on occupational psychiatry, and has sponsored events at annual meetings for psychiatrists interested in occupational psychiatry.

# The Council on Internal Organization

Donald J. Scherl, M.D., Chairperson

The council oversees "all those matters involved in the organizational structure of the Association not covered by constitutional committees." There are 11 components that report directly to the council and 16 components that report to committees under the council, primarily award boards and subcommittees of the Scientific Program Committee. The council thus has responsibility for a wide range of activities: maintenance of the APA headquarters; benefits offered to members, such as the legal consultation plan; program content, exhibits, and arrangements for annual meetings; advertising policy; data processing, telecommunications, and other information systems within the Association; various prizes and awards given by APA in recognition of outstanding achievement; personnel and staff benefit programs; and the federation of auxiliary organizations. Following are the highlights of council and component activities over the past year.

The *Scientific Program Committee*, Allan Tasman, M.D., chairperson, reported that the 1989 annual meeting, which had 15,000 registrants, broke all previous records for participation at APA annual meetings and had the largest attendance of APA members ever. The committee's budget for its three outside lecturers was increased to be more competitive with those of other organizations. Dr. Tasman also raised the matter of providing sign language interpreters for hearing-impaired individuals attending APA meetings. A limited trial program for APA members will be in place for the 1990 annual meeting.

The *Committee on Advertisers and Exhibitors*, Henry H. Work, M.D., chairperson, reported that the *Daily Bulletin*, which had been published during annual meetings by a pharmaceutical company, will be brought in-house beginning in 1990. This step has been taken to improve the accuracy of the information included in the bulletin and ensure sufficient publicity for program changes. Other changes for the 1990 meeting are 1) implementation of the December 1988 Board of Trustees policy that states, "Organizations or companies that discriminate in recruitment or employment on the basis of gender, race, religion, or sexual orientation will be prohibited from recruiting or offering employment in APA exhibit areas" and 2) a policy for handling members' complaints of discrimination.

The *Committee on Advertising*, William D. Strathmann, M.D., chairperson, serves as an advisory board to APA's three periodicals (*Psychiatric News*, *American Journal of Psychiatry*, and *Hospital & Community Psychiatry*) on questionable advertisements either submitted for publication or being considered for solicitation for publication. The committee works closely with the Committee on Advertisers and Exhibitors to keep the latter informed about advertisements it recommends for rejection. The guidelines for acceptance of advertisements are being reviewed by the committee, which anticipates that draft revisions will be presented to the council in 1990.

The *Committee on Friends of the APA*, Evelyn P. Ivey-Davis, M.D., and V. Terrell Davis, M.D., cochairpersons, reported that the APA Auxiliary presented a resolution to the Assembly in May 1989 that calls on APA officials, in collaboration with the American Medical Association, to establish programs designed to educate and enlighten the citizenry of our country regarding mental illness.

The *Committee on Grants and Awards*, Alan I. Levenson, M.D., chairperson, approved two new awards: the Nancy C.A. Roeske Certificate of Recognition for Excellence in Medical Student Education, proposed by the Council on Medical Student Education, and the Wisniewski Young Psychiatrist Award. Still being considered are a human rights award, proposed by the Committee on Human Rights, and a public affairs network award, proposed by the Joint Commission on Public Affairs. Procedures for present awards were refined, and improved methods for maintaining the solvency of award board funds were reviewed.

The *Committee on History and Library*, Garfield Tourney, M.D., chairperson, held a component workshop at the University of California, San Francisco, in May 1989, which drew about 50 people. The "History Notes" column in *Psychiatric News* continues to be a success, and additional interviews are being scheduled for the ongoing oral history project involving past APA leaders. In the library, three new databases have been added, and a disaster recovery plan has been completed.

The *Committee on Information Systems*, Zebulon C. Taintor, M.D., chairperson, has been relatively inactive in recent years. However, Dr. Taintor and the committee plan to become more active in developing and reviewing current in-house and member computer needs.

The major project of the *Committee on Special Benefit Programs*, George L. Mizner, M.D., chairperson, is the financial planning services program, which was approved by the Board of Trustees in December 1988. The committee hopes to have a pilot program in place shortly, and it will later expand into other parts of the country. The committee is also planning a seminar on career choices in psychiatry for fall 1990.

The *Committee on Telemedical Services*, Jane H. Preston, M.D., chairperson, monitors the progress of interactive video and discusses the legal and educational standards involved. After consultation with the AMA Section Council on Psychiatry, Dr. Preston began working with the AMA Council on Medical Services to encourage that council to become more actively involved in this area, particularly in the area of licensing interstate interactive video.

The *Headquarters Committee*, Raymond I. Band, M.D., chairperson, is charged with oversight of the APA headquarters building and has been inactive in recent years. The council feels the committee is important for protecting the members' investment in the building. The committee has been rejuvenated and is examining its role.

The *Personnel Committee*, Maurice J. Martin, M.D., chairperson, felt that APA pension benefits were not competitive with those of other organizations in the Washington, D.C., area. The Board approved monies for improved retirement and savings benefits, and the committee endorsed creation of a defined benefit pension plan with these funds. This plan will complement the existing 401(k) plan. The committee is now examining staff leave policies, a drug-free workplace policy, and a mutual respect policy (covering sexual and other forms of harassment).

In addition, the Council on Internal Organization considered information from APA's Division of Government Relations concerning the proposed federal income tax on profits from an unrelated business and what it would mean to APA. In its meeting with the Joint Commission on Government Relations, the council suggested that APA examine the issue of children who grow up amid crime and violence and the generation of people whose development has been affected by these circumstances. This is an issue for all of APA's components.

Also discussed was a proposal to work toward a commemorative stamp honoring psychiatry in 1994, the 105th anniversary of APA. This was referred to the Joint Commission on Public Affairs and to a committee, approved by the Board but not yet appointed at the time of this discussion, for organizing activities during the 1994 annual meeting related to this anniversary.

In summary, the Council on Internal Organization continues to represent the members in the business and internal workings of the Association. It welcomes all input and comments from members.

# The Council on International Affairs

Paul J. Fink, M.D., Chairperson

The Council on International Affairs deals with questions pertaining to psychiatry, mental health, and other APA concerns that have international aspects. Its purview includes, but is not limited to, organizational, scientific, and educational activities and matters of public policy. It provides guidance to APA staff on matters having international implications, liaison with other APA components dealing with matters international in scope, and reports to APA on new or evolving roles and responsibilities in the field of international affairs. The planning of all international congresses and conferences is also the responsibility of this council.

The council is pleased with the inclusion of additional wording in APA's "Statement of Mission, Goals and Objectives" that provides a more international scope to APA's activities. With a new council chairperson, a main topic for discussion this year has been the future directions of APA's international activities. APA has a certain role in world psychiatry, and many individuals and organizations in other countries look to APA for collaboration and communication. Dr. Fink would like to heighten APA members' knowledge of our international activities, as this area is often misunderstood. Some of the main goals of our international efforts are establishment of networks around the world to further communication among psychiatrists and psychiatric organizations in all countries, international education, patient referrals in other countries, fighting psychiatric abuse, and protecting human rights. The council hopes that these activities will expand in the future to include faculty exchanges, trainee exchanges, further fund-raising, an international travel service for members, and a newsletter from the Office of International Affairs to further communication and understanding among APA members and psychiatrists in other countries.

The council is pleased with actions taken at the VIII World Congress of Psychiatry (WPA) in Athens in October 1989 and the restructuring of the WPA. New statutes and bylaws were accepted, creating a new eight-member Executive Committee and allowing for a General Assembly meeting every 3 years. A slightly modified voting structure was adopted and will give more voting power to the smaller organizations. The Committee to Review Abuses of Psychiatry was strengthened in the statutes, and a new Operational Instrument will allow for more effective functioning of this important committee. APA is pleased with the new slate of WPA officers, who have staggered terms to maintain continuity:

President—Dr. Jorge Alberto Costa e Silva, Brazil
President-Elect—Dr. Felice Lieh-Mak, Hong Kong
Secretary General—Dr. J.J. Lopez-Ibor Alino, Spain
Secretary for Finance—Dr. John Grigor, Australia
Secretary for Meetings—Dr. Harold Visotsky, United States
Secretary for Editorial Policy—Dr. Janos Furedi, Hungary
Secretary for the Committee—Dr. Carlo Cazzullo, Italy
Secretary for Sections—Dr. Allan Beigel, United States

We are also pleased with the excellent representatives on the 15-member Advisory Committee, including two APA members from Canada, who represent the North American area: Drs. Quentin Rae Grant and Jean-Yves Gosselin.

A more controversial issue brought for vote by the General Assembly was the admission of the All Union Society of Psychiatrists and Narcologists of the U.S.S.R. into the WPA. This society resigned from membership in the WPA in 1983 to avoid suspension or expulsion at the 1983 world congress in Vienna. Its letter of resignation criticized APA and other societies for politicizing psychiatry by accusing the All Union Society of using the profession for political purposes. At the 1989 world congress, the All Union Society sent a letter to the Royal College of Psychiatrists of the United Kingdom and to APA stating that "the All Union Society unreservedly withdraws the statement referring to the Royal College of Psychiatrists and to the American Psychiatric Association as contained in the letter addressed to all member societies of the WPA (31/01/1983) signed by G. Morozov. It was emotional and incorrect. The All Union Society expresses its regrets to the WPA, to the American Psychiatric Association and to the Royal College of Psychiatrists." In addition, the All Union Society made the following statements:

1. The All Union Society of Psychiatrists and Narcologists of the USSR publicly acknowledges that previous political conditions in the USSR created an environment in which psychiatric abuses occurred for non-medical reasons, including political.
2. Victims of abuse shall have their cases reviewed within the USSR, and also in cooperation with the World Psychiatric Association, and invites the Review Committee to the USSR as soon as possible for such issues. The psychiatric registry shall not be used against psychiatric patients. One million patients within the last years were taken off from the register.
3. The All Union Society unconditionally accepts the WPA Review Committee Operational Instrument which was unanimously approved by the WPA General Assembly.
4. The All Union Society supports the changes in the Soviet law with the full implementation relevant to the practice of psychiatry and the treatment and protection of the rights of the mentally ill. New mental health law is in preparation in the USSR.
5. The All Union Society encourages an enlightened leadership in the psychiatric professional community in the Soviet Union.

After this statement was read to the delegates to the General Assembly, the following resolution was raised and accepted:

> Whereas the Delegate of the All Union Society of Psychiatrists and Narcologists of the USSR has made a statement incorporated in this motion;
>
> Whereas the WPA is already on record that it will accept as full members only those Societies that subscribe to the Review Instrument;
>
> Be it resolved that the All Union Society of Psychiatrists and Narcologists of the USSR be accepted into membership on the following conditions:
>
> A site visit by the WPA Review Committee be made in one year;
>
> If the report of the Review Committee indicates that psychiatric abuse continues, a special session of the WPA General Assembly will be convened to consider suspension of the All Union Society of Psychiatrists and Narcologists of the USSR

The Independent Psychiatric Association of the U.S.S.R. and a number of organizations in other countries were accepted as new members without conditions.

We are confident that under this new WPA Executive Committee and structure and with a strengthened Review Committee and renewed commitment to medical ethics in the WPA, the organization can truly take on the leadership role in international psychiatry for which it was established many years ago.

APA cosponsored an unprecedented visit to the Soviet Union in February and March of 1989 with the U.S. State Department and the National Institute of Mental Health to look into the current state of Soviet psychiatry, with particular emphasis on psychiatric abuse. The Soviet Ministries of Foreign Affairs and Health organized the visit from the Soviet side and facilitated interviews by a delegation of 19 psychiatrists, lawyers, and human rights specialists of former and present psychiatric patients interned on political charges and visits to four psychiatric hospitals, including two "special psychiatric hospitals." A full report of the findings of this delegation and the Soviet response was released in July 1989. Negotiations regarding a visit to the United States by a similar Soviet team are under way.

The council continues to be involved in the International Scholars Program for APA annual meetings and was pleased that the Office of International Affairs could establish an international visitors booth at the San Francisco meeting. Staff at this booth answered over 1,600 inquiries by individuals from 42 different countries. There were approximately 1,225 visitors from abroad at that meeting.

The *Task Force on International Education*, Normund Wong, M.D., chairperson, has facilitated an agreement between APA and the International Medical Scholars Program whereby APA serves as the psychiatric component for this important project. This program facilitates specialized training in the United States for qualified mid-career psychiatrists from other countries, who visit for 6 months to 3 years and then return to their countries of origin. The program is now accepting applications from institutions in other countries on behalf of qualified candidates. APA will work with the applications from psychiatrists and make recommendations to the program for action, identify U.S. training programs that are interested in participating, and attempt to appropriately match the accepted scholars with these programs. APA will then work with the centers and scholars to ensure that the training is appropriate and directly relevant to the work of the scholar in his or her home country. APA is enthusiastic about this important project and its collaboration with the International Medical Scholars Program. The task force believes it has fulfilled its charge and asked that it be disbanded and replaced by a committee to fulfill APA's obligation to the program.

The *Committee on Abuse and Misuse of Psychiatry and Psychiatrists*, Joseph Bloom, M.D., chairperson, continues to be very active, having regular meetings and conference calls every 6 months. The charge of this committee is to review complaints of abuse and misuse anywhere in the world, to refer appropriate cases to the WPA Committee to Review Alleged Abuse of Psychiatry, to make recommendations to the APA Board of Trustees regarding actions to be taken on behalf of certain individuals believed to be victims of abuse, and to collaborate with other international organizations in the investigation of cases. One main focus of the committee in this past year has been to evaluate the situation regarding psychiatric abuse in the Soviet Union and to make suggestions on actions to be taken by the APA leadership at the World Congress of Psychiatry in Athens. The strengthened WPA Review Committee and its new Operational Instrument were originally proposed by the APA Committee on Abuse of Psychiatry, which also worked diligently on proposals for APA resolutions related to the admission of the All Union Society of Psychiatrists and Narcologists of the U.S.S.R. into the WPA. The committee believes that it should continue to carefully monitor the situation in the Soviet Union and to facilitate the work of the new WPA Committee to Review Abuses of Psychiatry. In addition, the committee will continue to work on individual cases of alleged abuse in a number of countries.

The committee welcomed the first U.S. visit of Dr. Semyon Gluzman, a Soviet psychiatrist and Distinguished Fellow of APA who was imprisoned in the Soviet Union from 1972 to 1982 for his activities directed against the use of psychiatry for political purposes in that country. Dr. Gluzman participated in the VIII World Congress of Psychiatry in Athens and was a guest of the Texas Association of Psychiatric Physicians and other U.S. organizations.

The committee continues to have a liaison with the APA Committee on Human Rights and Committee on Abuse and Misuse of Psychiatry in the U.S.

The *Committee on Human Rights*, Lawrence Hartmann, M.D., chairperson, concerns itself with the psychiatric consequences for individuals and their families of human rights violations involving extreme, unusual, and cruel methods of incarceration and punishment, i.e., terror and/or torture. It also makes recommendations to the APA Board of Trustees on any actions deemed appropriate. Dr. Hartmann participated in a mission to South Africa in April 1989 to assess the effects of apartheid on the medical care system of that country; the mission was cosponsored by the American Association for the Advancement of Science, the American College of Physicians, and the Institute of Medicine. APA is pleased to cosponsor such missions and the committee would like to have more fund-raising by APA staff to facilitate more activities of this kind.

The committee has proposed the following resolution regarding South Africa:

> The APA continues to be firmly opposed to apartheid, and urges APA members and others to be educated about and to speak out against apartheid.
>
> We encourage APA members to learn about South Africa and the positions and actions of any individual South Africans and South African organizations with whom/which they interact. We urge them to be selective in ways they consider likely to help end apartheid; for instance, by helping the many South Africans who are working to end apartheid. We urge any APA members who take part in scientific meetings in South Africa to find prominent ways of speaking out against apartheid at those meetings.
>
> The APA urges its members and their institutions, when inviting South Africans to America, to be sensitive to achieving an appropriate balance between non-white and white South Africans.
>
> The APA Committee on Human Rights and the Office of International Affairs will be available to help with education on these issues.

At the time this report was written, the resolution had been passed by the Joint Reference Committee and was awaiting decision by the Board of Trustees in December.

The committee has looked at medical and psychological abuses in many other countries this year, including China, Bulgaria, Israel, Iraq, Bahrain, Cuba, the Soviet Union, Hungary, Afghanistan, Tibet, Chile, Argentina, Turkey, and Romania. On occasion, the committee writes letters of inquiry about specific cases but more often serves as a liaison with other organizations in various governmental and nongovernmental efforts to improve these situations.

The committee has initiated resolutions before the House of Delegates of the American Medical Association (AMA) to encourage the AMA to become more active in the human rights arena. APA will continue to work with the AMA and other organizations to increase the involvement of medical and scientific organizations in human rights efforts. In addition, the committee has proposed a new APA human rights award to bring attention to individuals and organizations around the world who have made outstanding contributions to human rights and medicine. The committee is presently working with the APA Committee on Grants and Awards to finalize this important award.

The committee is exploring ways to increase its effectiveness and is discussing its future directions. There is a possibility that the committee may more actively support the centers for the treatment of torture victims around the world and advocate training in this area.

The *Task Force to Plan the Joint Meeting With the German Society of Psychiatry and Nervous Diseases*, Eric Plaut, M.D., chairperson, is working with its German counterpart on the scientific program for this meeting, which will be held Sept. 29–30, 1990, in Bonn, West Germany, immediately after the biennial meeting of the German society scheduled for Sept. 27–28, 1990. There will be satellite symposia Oct. 1–2 in Mainz, Oct. 2–4 in Mannheim and Heidelberg, and Oct. 4–5 in Munich. Some of the topics to be covered at this meeting include the historical aspects of German psychiatry; childhood, adolescents, and violence; *DSM-IV* and *ICD-10*; innovative psychopharmacology; genetics; drug abuse; adaptation of immigrants in the 1990s; paying for mental health care; and advanced technology in psychiatry. There will be an outstanding scientific and social program, and APA members and others are urged to participate in this special event.

The *InterAmerican Council of Psychiatric Organizations*, Rodrigo Munoz, M.D., APA delegate, continues to increase communication and understanding between psychiatrists and psychiatric organizations in the Americas. They have organized and presented "Psychiatry in the Americas" symposia at major psychiatric meetings, including the APA annual meetings and the VIII World Congress of Psychiatry in Athens. The InterAmerican Council has continued to operate because of the individual commitment of its members, since there is no budget to support the activities.

The *Task Force on Conflict Resolution* has been approved by the APA Board of Trustees, but to date no appointments have been made. The purpose of this task force is to explore psychiatry's role in the understanding of conflict generation, conflict negotiation, and conflict resolution and to propose an ongoing project for APA in this area. The focus of the task force's work was to be conflicts between nations or subnations. The task force would build on the work done by other APA task forces and would eventually take over the work of the *Task Force on the Psychological Aspects of the Middle East Peace Process*, which has been inactive in the past several years because of the lack of funding.

At the time of this writing, the Joint Reference Committee had approved the council's proposal that there be a joint meeting in the Caribbean immediately after the APA annual meeting in New Orleans in 1991. This requires a waiver of the APA regulation stating that joint meetings in other countries can only be held every 2 years. The council believes that this would be a particularly good time for a meeting in the Caribbean and that it would be of special interest to our members. The council also reminds APA members that there will be a joint meeting with the Royal College of Psychiatrists of the United Kingdom in 1992.

# The Council on Medical Education and Career Development

Jerald Kay, M.D., Chairperson

The primary responsibility of the council is to guide medical education for psychiatrists. As part of this function, the council and its components offer recommendations to APA on psychiatric education for medical students, residents and fellows in psychiatry, and practicing psychiatrists. In addition, recruitment of high-quality medical students into psychiatry and the career development of psychiatrists are major functions of this council. The council comprises 18 components, each of which considers issues related to psychiatric education and career development.

1. *Proposed component on issues involving psychiatrists in later life.* Dr. Bernice Elkin met with the council to discuss the results of a survey she conducted on retirement by psychiatrists aged 55 and older. She found that the majority of those younger than 80 continue to practice psychiatry. Dr. Elkin noted that many changed career focus in later years, and some were unhappy about having been forced to retire from academia. Many older psychiatrists joined the staffs of local, state, and Veterans Administration (VA) hospitals, while others continued private practice with a reduced schedule or entered group practice for the first time. Dr. Elkin pointed out the limitations of her survey and was not aware of any other extensive research concerning the careers of older psychiatrists. The council will work with Dr. Elkin in expanding the scope of this project as background for its consideration of recommending creation of a new component on psychiatrists in later life.

2. *Critical incidents.* The council continues to assist with the activities of the group planning a critical incidents study for psychiatry. A proposal for assembling selected samples of critical incidents is under development and will be presented to foundations in an effort to obtain approximately $200,000 to fund this project. The project will be housed under the Council on Medical Education and Career Development and receive support from the Office of Education. The American Academy of Child and Adolescent Psychiatry has also established a work group on developing standards of care, which is conducting a survey. It is hoped the results will be shared with APA through this council.

3. *Work Group on Disclosure of Confidential Personal Information.* A work group was formed this year to focus on concerns about confidentiality, disclosure, and the implications of disclosure of physicians' psychotherapy. The group, made up of representatives from council components, reviewed information about physicians, mental illness, and treatment that is requested on current applications for licensure, admission to medical schools and residency training programs, insurance, and hospital credentials. It will consider development of APA position statements on disclosure of such information.

The group has thus far recommended following the principle that physicians should not be asked about past conditions or treatment but may be questioned about their present mental health. This principle is consistent with the American Medical Association (AMA) policy statement on licensure confidentiality approved in 1988. APA had significant input into the preparation of the AMA statement. Two additional meetings will be held to prepare detailed guidelines for consideration by the council in September 1990.

4. *Child and adolescent psychiatry recruitment conference.* The council has reviewed the report on the Child Recruitment Conference held in January 1989 by the American Academy of Child and Adolescent Psychiatry, American Association of Directors of Psychiatric Training, American Association of Chairmen of Departments of Psychiatry, Association for Academic Psychiatry, and the Society of Professors of Child and Adolescent Psychiatry and deferred extensive discussion on this issue to the 1990 summer retreat, when input will be sought from the Committee on Graduate Education, the Committee on Medical Student Education, and the Committee of Residents.

5. *Accreditation Council for Graduate Medical Education issues.* The council reviewed the minor revisions to the general requirements of the Accreditation Council for Graduate Medical Education and found no significant changes affecting psychiatry. The council felt that the document was an improvement on the earlier version and recommended APA approval.

In reviewing the revised general requirements, the Committee of Residents and the Committee on Graduate Education realized that there were no statements regarding resident safety. The council felt it is important for the accreditation council to begin to address this issue and recommended APA communicate to that council, by way of the Council of Medical Specialty Societies, that the following should be included as item II.F.1.g. of the general requirements: "Procedures for assuring resident safety which include, but are not limited to, providing a weapon-free and safe environment, and adequate training in the identification and management of the violent patient."

The Accreditation Council for Graduate Medical Education will appoint a committee to write a proposal for how to handle requests for accreditation of subspecialty fellowships that do not lead to certification by the American Board of Psychiatry and Neurology (ABPN).

6. *Liaison with the Task Force on Education and Training in Geriatric Psychiatry.* The council met with representatives of the task force to discuss developing a model curriculum for geriatric fellowship programs, reviewing the content of geriatric psychiatry education in general residency programs, and developing a continuing education program for practicing psychiatrists. The council suggested a) that the task force initially prepare a document containing goals and objectives for each task, a list of suggested readings, and a list of existing educational programs, b) that a psychiatric educator with experience in curriculum development be included on the task force, c) that the task force develop strong links with the American Association of Directors of Psychiatric Residency Training Committee on Curriculum, and d) that the task force keep the council informed of its progress.

7. *Liaison with the Commission on AIDS.* The commission met with the council to solicit suggestions, increase awareness, and establish liaisons with the psychiatric education community. The council suggested that the commission a) sponsor a workshop at the January 1990 meeting of the American Association of Directors of Psychiatric Residency Training, b) contact the American College of Psychiatrists to see if more material on the acquired immune deficiency syndrome (AIDS) can be incorporated into the Psychiatry Residency In-Training Examination (PRITE), c) contact the National Board of Medical Examiners to see if more AIDS-related questions can be included in the psychiatric sections of its part I and II examinations, d) work to establish more continuing medical education (CME) on AIDS and encourage more coverage of AIDS in the *American Journal of Psychiatry* and *Psychiatric News*, e) forward the results of the resident survey on AIDS instruction to the Committee of Residents and the Committee on Graduate Education for their review and comment, and f) establish informal liaisons with these council components and with the Committees on Continuing Education and the Impaired Physician.

The *Committee on Administrative Psychiatry*, Stephen Rachlin, M.D., chairperson, reported the results of the administrative psychiatry oral examination, which took place on May 6, 1989, at the Langley Porter Institute for Psychiatry at the University of California, San Francisco. Of the 15 individuals examined, eight passed and have been certified by the committee, three conditioned, and four failed. The committee announced that Dr. Stuart Keill is the recipient of the 1990 Administrative Psychiatry Award. The committee has also discussed and approved the revised application for certification, reviewed the candidates' performance on the 1989 written examination, discussed the penultimate versions of the policy and procedure manual for the examination, begun revision of the forms used during the oral part of the examination, and noted the paucity of training opportunities in administrative psychiatry.

The *Committee on Consultation-Liaison Psychiatry and Primary Care Education*, Thomas Wise, M.D., chairperson, asked the council to consider whether another council, such as the Council on Psychiatric Services, would be a more appropriate umbrella for this committee since it deals with many issues beyond medical education and career development. The council was unanimous in its response that the committee should stay under this council and continue to operate as a clearinghouse and receptor, as opposed to a consortium.

The council was given a historical overview of the events that preceded the first meeting of the National Consortium on Consultation/Liaison Psychiatry. Issues of current concern for this committee include committee structure and membership, delineation of issues, and the committee's relationship to other organizations involved with consultation-liaison. The council suggested that the committee 1) review its structure and membership in light of council discussions and meetings held by other groups and make changes as appropriate, 2) contact as many other appropriate APA components as feasible in carrying out activities, 3) continue to monitor the activities of other organizations involved with consultation-liaison, especially the leadership group coordinating the efforts of the various organizations, and 4) carefully consider accreditation of fellowship programs as one of its primary roles for the future.

Dr. Wise reviewed with the council the committee's extensive discussions on the need to refocus its efforts and reduce its size, and the following goals and objectives were outlined: the new focus will remain within APA's scope, the committee will remain neutral on subspecialization, assistance will be obtained from the APA Survey Design and Analysis Department to determine the number of consultation-liaison psychiatrists, and liaisons will be established with the Councils on Economic Affairs and Psychiatric Services.

The committee also discussed the Dista Products Company educational project involving psychiatry and primary care and the more general issue of the role this committee might have in reviewing such projects. As a result of this discussion, the committee recommended, and the council endorsed, adoption of a policy concerning primary care education activities, a revised version of which will be reviewed by the Joint Reference Committee in 1990.

The *Committee on Continuing Education*, John Goethe, M.D., chairperson, asked for reinstatement of $2,000 for the audiovisual library. The council reviewed and revised the committee's charge to reflect realistic goals and expectations for future activities. Dr. Goethe presented the council with a brief list of educational or education-related activities conducted by APA components and councils to demonstrate the need for coordinating educational efforts in APA. Arguments for and against this project were made, and the council directed Dr. Goethe to discuss this issue with the committee and return to the council at the fall component meetings with its recommendations. The council also suggested that the committee develop guidelines for CME self-directed study.

The *Committee on Graduate Education*, Stefan Stein, M.D., chairperson, reported on several issues to be further discussed by the council in 1990. The committee strongly opposes the use of PRITE scores for review of programs by the Residency Review Committee for Psychiatry and asked the council to affirm this position. The committee strongly supports, and asked the council to endorse, a pilot program by the ABPN to move eligibility for part I of the certifying examination to the fourth postgraduate year, which would allow residents to take the examination; details of the program would be determined by the ABPN. The committee also reviewed and discussed several questions regarding special qualifications for psychiatrists treating adolescents and recommends no change in policy.

The committee reviewed, and the council endorsed, support for resolution 12 from the AMA House of Delegates meeting in June 1989, "Non-Discrimination Toward Medical School and Residency Applicants on the Basis of Sexual Orientation."

The committee suggests that the curriculum on the chronically mentally ill be included in the American Association of Directors of Psychiatric Residency Training reference library of model curricula. The committee strongly supports the revised and expanded version of the curriculum for learning about homosexuality and suggests that the council promote inclusion of this topic in a future annual meeting Psychiatry Update presentation. Dr. Stein will pursue this further with the Scientific Program Committee.

The committee also recommended that the Residency Review Committee for Psychiatry adopt the guidelines for resident work hours and on-call duty outlined in a letter by Dr. James H. Shore. The council will review this issue further.

The committee endorsed the work of the Committee of Residents concerning resident safety in VA settings and urges continued support for the work of the Task Force on Clinician Safety.

The *Committee on the Impaired Physician*, Malkah Notman, M.D., chairperson, has brought many projects to closure and presented to the council a new draft of "Guidelines for the Psychiatric Care and Treatment of Medical Students and Residents." The council recommended that this document be reviewed by the Committee on Graduate Education and the Committee of Residents before it is presented to the Joint Reference Committee. This document can be produced as a pamphlet or a paper and could be published in a journal. The committee requested, and the council approved, the permanent establishment of liaisons between this component and the Committee on Graduate Education and the Committee of Residents. The committee hopes to develop an educational videotape on young physicians recovering from alcohol and substance abuse.

Dr. Notman also presented a draft of "Guidelines to District Branches for Physician Impairment" for review. The committee reviewed the most recent draft of "Interim Guidelines for Physicians Who Are HIV Infected"; it wholly endorses the draft and commends the Commission on AIDS for its excellent work.

The *Committee on Independent Study*, Theodore Nadelson, M.D., chairperson, reported that Dr. Johannsen has stepped down as chairperson of this committee because of a continuing illness, and Dr. Nadelson has been appointed as his successor. The committee continues to 1) develop educational materials for a workbook titled *Mood Disorders*, 2) develop a series of articles for *Psychiatric News* on computers in psychiatry, with emphasis on self-study, 3) develop a hands-on computer workshop at the 1990 APA annual meeting, 4) explore the possibility of a survey of members' self-study habits, and 5) explore possible study program for blind physicians.

The committee discussed new ways to reach out to the membership on issues concerning independent study, and the committee proposed a new semiannual column for *Psychiatric News*.

After considerable discussion on the roles and future directions of both the Committee on Continuing Education and the Committee on Independent Study, the council has recommended that the Committee on Independent Study be disbanded and that its remaining functions be incorporated into the charge of the Committee on Continuing Education.

The *Committee on Medical Student Education*, Leah J. Dickstein, M.D., chairperson, reported great pleasure about the success of the first Medical Student Day at the 1989 annual meeting. Approximately 120 medical students, residency training directors, and APA leaders came to the first annual Medical Student Luncheon, which was sponsored by the Burroughs Wellcome Company. The committee asked and received approval from the council to hold another Medical Student Day in 1990. The committee's plans for the 1990 annual meeting include another luncheon and a resource booth for medical students and residents, if assistance in staffing the latter can be obtained from a New York medical school. Additionally, the Board of Trustees approved the establishment of a hospitality suite for medical students and residents to provide them with a place to meet informally and exchange information. The committee also agreed to hold special workshops on Medical Student Day that would be of particular interest to medical students.

In conjunction with the council's work group on disclosure, the committee will develop guidelines for the psychiatric treatment of medical students, focusing on competence to work.

The committee has recommended that medical student dues be standardized, both nationally and at the district branch level, to further increase medical student participation in APA, particularly in district branches, where medical student fees discourage membership.

With the tremendous success of *Psychiatric Residents as Teachers* in 1988, the committee has asked for and been granted approval to distribute more copies to new residents over the next 3 years.

Dr. Dickstein reported that a subcommittee has been established within the component to implement the Nancy Roeske Award, which has been approved by the Board. Implementation is expected in 1990.

The committee discussed the degree of staff effort involved in producing the *Clearinghouse on Medical Student Electives* and noted that fewer than 200 copies are distributed annually. The committee therefore asked for, and the council approved, abolition of this booklet and incorporation of its content into the *Directory of Psychiatry Residency Training Programs* to keep the information available and minimize staff labor.

Dr. Dickstein cited the need to strengthen liaison with the Student National Medical Association, as well as maintain relations with the American Medical Student Association.

The *Committee on Psychiatrist Leadership in Public Mental Health Programs*, Robert Leon, M.D., chairperson, distributed "Survey of Psychiatrists in the State Mental Health System" and concluded that no additional follow-up is warranted at this time. The council also reviewed with Dr. Leon the status of "Standards and Guidelines for the Chief Executive Officer and the Medical Director," which was developed by the committee, and agreed that more work is needed before the guidelines can be submitted for APA approval.

Because there were no recommendations for future activities for this component, the council recommended that the committee be disbanded and that any follow-up on its past activities be referred to other APA components. The committee was thanked for its consistently excellent work over the years in promoting administrative psychiatry.

The *Committee of Residents*, Michelle Riba, M.D., chairperson, sought and received approval from the council to seek outside funding of a resource booth at the APA Resource Center at the annual meeting for Members-In-Training and Medical Student Members. The committee feels that the resource booth and hospitality suite will provide a place for residents and medical students to obtain useful information about APA, as well as the opportunity to hold informal discussions. Such resources may increase the annual meeting attendance of both Members-In-Training and Medical Student Members.

The committee explained to the council that the addition to "The Principles of Medical Ethics With Annotations Especially Applicable to Psychiatry" concerning sexual involvement between supervisor and patient needed to be publicized. It was recommended that the standard be forwarded to the American Association of Directors of Psychiatric Residency Training for its review and comment and publication in its newsletter. The council stressed that residents should also be included in and be expected to abide by these ethical standards.

The Committee of Residents' experience over the past few years has shown that committee members often pursue fellowship training during their committee tenure and that trainees in subspecialty fellowships may not often be completely enfranchised in APA. The committee therefore recommended, and the council endorsed, a change of the name of the Committee of Residents to Committee of Residents and Fellows, so that the name more accurately reflects the composition of the committee.

The committee shares the concern of the Committee on Graduate Education about clinician safety and feels that residents must receive training in aggression management to learn how to effectively deal with violent patients. The issue of threats and assaults by patients has surfaced repeatedly and appears to be a chronic problem facing residency training programs. The council concurred with this sentiment and recommended that an emergency motion be forwarded to the Board of Trustees concerning the general requirements of the Accreditation Council for Graduate Medical Education for protection of residents against patients' violence.

The *Committee of Young Psychiatrists*, David Whitehouse, M.D., chairperson, reported that the committee sought and received council endorsement of a proposal to the AMA to study the demographics of board certification. The council agreed to forward this proposal to the AMA Section Council on Psychiatry for its review and approval.

The committee also stated its unanimous support for recertification and encouraged the council to support efforts to study the effect of any barriers to certification or recertification.

The committee recommended that the Medical Director send a congratulatory letter to graduating residents to welcome them to General Membership and "young psychiatrist" status (and possibly include a brief description of the committee), to notify them that their member dues will increase, and to invite them to contact APA about any concerns regarding their member status transition. The committee also recommended that graduate dues not be increased by $200.00 for the first few years but instead increase by $150.00 in years 1 and 2 and by $250.00 in years 3 and 4; it also suggested that payment options be printed on dues bills, indicating dues could be paid in quarterly, semiannual, or annual installments. The council urged the committee to discuss dues revision with the Committee on Membership and report back to the council.

The *Steering Committee, Psychiatric Knowledge and Skills Self-Assessment Program VI (PKSAP VI)*, Gordon Strauss, M.D., chairperson, reported that module B of PKSAP VI was mailed in May 1989 and the deadline for return was extended to Oct. 31, 1989. Unforeseen complexities in the distribution of module B caused some delay and required special handling of inquiries by the Office of Education staff and American Psychiatric Press, Inc. It is anticipated that module C will be mailed by March 31, 1990.

The *Task Force on Educational Activities for Diagnostic Systems*, Michael Fauman, M.D., chairperson, recommended a preliminary survey, which has been revised and retitled the "Diagnostic Practice Survey," on the use of *DSM-III-R* by practitioners; the council approved this survey. The task force also asked for and received approval for completion and distribution of the *Discussion Leader's Guide for DSM-III-R* through the Office of Education. The council also approved the task force's request to seek permission from Sinai Hospital in Detroit to use video vignettes filmed there with the *Discussion Leader's Guide*. Dr. Fauman also suggested, and the council approved, changing the task force's name from Task Force on Educational Activities for DSM-III-R to the Task Force on Educational Activities for Diagnostic Systems.

The *Task Force to Facilitate Communication Between APA and the ABPN*, Richard I. Shader, M.D., chairperson, recommended to the Ad Hoc Committee to Develop a Slate of Candidates for Election to the ABPN that it should gather additional information from potential nominees before making final recommendations to the Board of Trustees and suggested using a questionnaire.

Dr. Shader announced that Dr. Stephen C. Scheiber has been promoted to Executive Vice-President of the ABPN and added that this title change more clearly reflects his current role within the ABPN.

Dr. Shader expressed concern that the process for communication between APA and the ABPN has become confused, for it is not clear when issues need to be communicated through this task force. Dr. Shader reminded the council that the main function of this component is to monitor and resolve potential areas of disagreement between APA and the ABPN, and he noted that future issues of mutual concern could include subspecialty certification and recertification, which may cause some APA members to feel disenfranchised. Given these possibilities, Dr. Shader proposed that the council consider disbanding this component because of the lack of substantive issues at present or reconstituting the component's membership. He further asked the council to be mindful of potential future issues, such as recertification and subspecialty certification, and the role of the ABPN liaison to the council when making this decision. The council agreed that the task force should remain active and recommended that its functions be more clearly defined through yearly review. The council further suggested that the component's member base be reconstituted to provide a broader perspective.

Dr. Shader announced the following informational items: 1) the ABPN will have an invitational conference on written examinations, 2) the ABPN will hire a research coordinator, 3) the ABPN will consider allowing the ABPN part I examination to be taken during residency and will communicate its recommendations to the council, 4) the child psychiatry, general psychiatry, and pediatrics triple board experiment will be expanded from 5 to 10 years, 5) any author of or contributor to a book on passing ABPN examinations will not be eligible to be an ABPN examiner for at least the next year or two after the book is published, 6) the ABPN will study whether any examiner who has been found to have committed an ethical violation or is under ethics review should participate in ABPN committees or function as a Board examiner, and 7) the ABPN has asked the APA Board of Trustees to submit five candidates (rather than three) for the 1990 vacancy for ABPN director and requested that the names be submitted alphabetically.

The *Task Force on Post-Residency Fellowship Programs*, George Pollock, M.D., chairperson, reported that a survey was done in June and 234 responses were initially received. After follow-up letters were sent, a total of 300 completed surveys were received. The data base compiled from the survey will be completed by the end of the year, and a draft report will be available before the 1990 annual meeting.

The *Task Force on Recertification*, Joe Tupin, M.D., chairperson, reported that recertification has widespread support among APA members. At its June 1989 meeting, the APA Board of Trustees approved sending the following statement to the ABPN: "The APA will ask the ABPN to work with the APA in developing models which could be considered for a voluntary recertification program consistent with the APA position statement on recertification."

The council members discussed methods of recertification that could be developed by the ABPN and how APA members might react to each method. Dr. Donald Langsley informed the council of what other specialty boards have done to assess clinical practice and some of the newest methods of assessing clinical skills being considered by the National Board of Medical Examiners, particularly the use of standardized patients with multiple examination stations.

Dr. George Ginsberg reported on the proposed New York state regulations for recredentialling physicians. The regulations would require licensed physicians to be recredentialled every third license (approximately 9 years) and are anticipated to take effect in 1991. The proposed recertification option from ABPN would help psychiatrists in New York state meet the recredentialling requirements. Of particular concern is the recredentialling of office-based practitioners. APA has had preliminary discussions with Dr. Aaron Satloff, a psychiatrist who is on the New York state committee responsible for recredentialling, concerning the possible use of PKSAP test questions in the New York process. No further actions by APA are contemplated at this time.

Between 9,000 and 10,000 APA members (30%) are not board certified. In response to an Assembly request, the task force unanimously recommended that, in conjunction with the Task Force to Facilitate Communication between the APA and the ABPN, it develop a mechanism to poll all or a representative sample of noncertified members to find out how APA could help them become certified by the ABPN. This proposal was approved by the council, and the task force prepared a survey and plans distribution in winter 1989–1990.

The *APA/Mead Johnson Fellowship Selection Committee*, James T. Barter, M.D., chairperson, reported that the committee met in June 1989 and selected 15 new APA/Mead Johnson Fellows. These new fellows and the 14 second-year fellows participated in the 1989 H&CP Institute in Philadelphia. The fellows organized several presentations, including a day-long program on psychiatric services for the hearing impaired.

The *Selection/Advisory Committee of the APA/NIMH Minority Fellowship Program*, Charles A. Pinderhughes, M.D., chairperson, reported that the minority fellows began the 1988 fall component meetings with individual group meetings, followed by a forum chaired by Dr. Emmanuel Garcia. They discussed the need for better communication among resident groups and continued discussions on ethical guidelines regarding sexual contact between residents and supervisors. The following day the NIMH-sponsored research symposium and joint orientation for residents were held. At the 1989 annual meeting, the fellows held a workshop titled "AIDS: The Impact of Race."

The *APA/Burroughs Wellcome Fellowship Selection and Program Committee*, Roger Peele, M.D., chairperson, reported that 10 new fellows have been selected from a pool of 45 nominees for the 1989–1991 program. At the 1989 annual meeting, the fellows presented the workshop "Love: A Four Letter Word in Psychiatry." Also during the annual meeting Burroughs Wellcome hosted a well-attended reception for all current and former APA/Burroughs Wellcome (formerly Falk) Fellows. The fellows continue to publish a quarterly newsletter and are currently preparing their 1990 annual meeting workshop.

# The Council on National Affairs

Lindbergh S. Sata, M.D., Chairperson

This council is responsible for matters of national interest to psychiatry and the patients it serves. Social and health-related issues that affect underrepresented groups in the general population and within the profession warrant particular attention by this council. To address these issues, the council works closely with representatives from the Assembly, APA staff, and relevant APA components while overseeing and assisting the 12 components reporting to the council.

At the request of Dr. James Trench and the Ad Hoc Committee on Subspecialization, the council reviewed this committee's draft report and concluded that subspecialization is inevitable and that APA should do its best to prepare its members. Most of the components under this council also studied the report and sent their comments to Dr. Trench.

In June 1989, Dr. Sata asked the council and its components to review their respective charges and to report to the council. Nearly all the components revised their charges, as did the council. The council asked the components to refine their revisions and to distinguish between goals and tasks. The council will discuss these revisions at its May meeting.

The *Committee on Abuse and Misuse of Psychiatry in the U.S.*, Jose M. Pena, M.D., chairperson, finished its white paper, "Abuse and Misuse of Psychiatry in the U.S.: The Need for an Institutional Ethics," which provides a working definition of abuse and misuse of psychiatry. It makes distinctions between abuse, unethical conduct, and poor practice. The council recommended its publication, with the proviso that the committee correct any and all inaccuracies and include in the final version whatever recommendations from other components this committee considers appropriate.

The committee discussed abuse and misuse of psychiatry in the federal prison system with Mr. Leonard Rubinstein of the Mental Health Law Project, Ms. Elizabeth Alexander of the National Prison Project, Dr. Jeffrey Metzner of the former APA Task Force on Jails and Prisons, Mr. Arthur Peabody of the U.S. Department of Justice, and Joel Klein, APA legal counsel. One of the problems in federal, state, and local jails and prisons is inadequate mental health care.

One solution seemed to be better recruitment and training of staff, which brought up the question of the role of psychologists in these settings. The important point seemed to be the degree to which an institution delineates the correctional from the health care functions of its staff. The meeting bore other fruit—the guests offered to serve as informal liaisons to the committee and volunteered their help with complaints of systemic abuse, the federal prison system, and litigation.

The *Committee of American Indian/Alaskan Native Psychiatrists*, David C. Foos, M.D., chairperson, continues to recruit American Indian medical students into psychiatry. At meetings of the Association of American Indian Physicians, committee members talk to medical students about psychiatry and APA and encourage them to consider this specialty.

The committee is also concerned about retention and attrition of American Indians in medical school and in psychiatry. Linda Cross, M.D., is considering research on this topic.

The *Committee of Asian-American Psychiatrists*, Francis G. Lu, M.D., chairperson, and the Pacific Rim College of Psychiatrists cosponsored an international symposium on psychiatric research in Asia on May 6, 1989, in San Francisco. The symposium drew 141 participants, including psychiatrists from Hong Kong, India, Japan, Korea, the Philippines, and Taiwan. Six speakers gave an overview of research on schizophrenia, mood disorders, and anxiety disorders in their respective countries. There were afternoon workshops on these topics. The committee is planning a second international symposium in 1992.

After an extensive discussion of the federal demonstration project allowing military psychologists to prescribe medication, the committee wrote to U.S. Senator Daniel Inouye (D-Hawaii) to express its grave concerns about this project. The committee also discussed the retraumatization of many Japanese Americans interned during World War II because of the delay in appropriating money for reparation.

The *Committee of Black Psychiatrists*, Claire M. Cohen, M.D., chairperson, raised funds for the Solomon Carter Fuller Award from black psychiatrists and from Mead Johnson Pharmaceuticals. In addition, Mead Johnson has agreed to print a brochure describing the award and listing past and present winners. The committee chose James P. Comer, M.D., for the 1990 Solomon Carter Fuller Award.

Diane Felder, M.D., will coordinate work on the proposal for a transcultural curriculum to be used in residency training programs. This is one of six proposals aimed at acquainting psychiatry residents with ethnic and other cultures in the belief that such knowledge would benefit both the residents and their patients.

The Council on International Affairs considered a proposal regarding an academic boycott of South Africa and asked this committee to review the proposal. The committee supports it but added that APA members should be wary of meetings in South Africa, which may be more propaganda than academic in their intent.

The *Committee on Foreign Medical Graduates*, Walter Weintraub, M.D., chairperson, discussed the recent changes instituted by the National Board of Medical Examiners and agreed to by the Educational Commission for Foreign Medical Graduates, which allow foreign medical graduates (FMGs) to take either the Foreign Medical Graduate Examination in the Medical Sciences or parts I and II of the National Board of Medical Examiners examination. Passing either test meets the examination requirement for certification by the Educational Commission for Foreign Medical Graduates.

Ms. Laurie Flynn, Executive Director of the National Alliance for the Mentally Ill, met with the committee to discuss the report on public psychiatry sponsored by that organization. The committee protested the anti-FMG comments in the report, and Ms. Flynn assured the committee that the National Alliance for the Mentally Ill did not intend to cast aspersions on the qualifications or the work of FMG psychiatrists. The committee and the National Alliance for the Mentally Ill will keep each other informed about their efforts in order to avoid similar contretemps.

In 1983 the House of Delegates of the American Medical Association (AMA) stated that any FMG currently licensed by any jurisdiction in the United States should not be denied endorsement of said license or denied reexamination when required because of the inability to document graduation from a school meeting standards and performance requirements equivalent to those of programs accredited by the AMA Liaison Committee on Medical Education. Further, the AMA supports state legislation that bars discrimination against FMGs. Notwithstanding, the Committee on Foreign Medical Graduates feels these AMA resolutions are ineffective and APA should support federal legislation that prohibits discrimination against a licensed FMG who wishes to get a license in another state.

On Oct. 14 and 15, Dr. Weintraub chaired the fifth regional meeting for FMG psychiatry residents. Dr. Marjorie Wilson, President of the Educational Commission for Foreign Medical Graduates, gave an update on that organization. Dr. Kishore Thampy spoke about FMGs as minority physicians. Drs. Donna Norris, Roberto Jimenez, Leah Dickstein, and Normund Wong spoke about blacks, Hispanics, gender, and Asian and Pacific Islanders, respectively. John Bonnage, Ph.D., talked about communicating affect across cultures. Dr. Weintraub spoke about training directors' dilemma regarding admission of FMGs, and Dr. Stephen Scheiber, Executive Vice-President of the ABPN, talked about the ABPN certification process. Dr. Carolyn Robinowitz spoke on FMGs and organized psychiatry. There are plans for another meeting in October 1990.

The *Committee on Gay, Lesbian, and Bisexual Issues*, Terry S. Stein, M.D., chairperson, discussed with the Committee of Residents how their training programs deal with homosexuality, gay men, and lesbians. Some programs still regard homosexuality as pathology; some do not deal with the issue at all. To compound the problem, there are not enough faculty who can teach residents about homosexuality. Furthermore, gay and lesbian residents feel they are in a precarious position because of their sexual preference and feel the need for support groups.

The committee also met with the Committee on Graduate Education, which had recommended some changes in the curriculum on homosexuality previously submitted by the Committee on Gay, Lesbian, and Bisexual Issues. They discussed producing a videotape to supplement the curriculum and proposed a biopsychosocial approach for this videotape.

Resolution 12 of the AMA urges "nondiscrimination toward medical school and residency applicants on the basis of sexual orientation." The committee supports this resolution and would like APA to issue a formal statement of support.

In response to a request from the Assembly, the committee reviewed the action item "The Role of the Psychiatrist When Requested to Provide Information about Patients for Security Clearance." The committee then sent its comments to Dr. Aron Wolf, chairperson of the Committee on Confidentiality.

The *Committee of Hispanic Psychiatrists*, Eduardo R. Val, M.D., chairperson, chose Dr. Guillermo Barrientos de Llano, Director of Mental Health Services of the Republic of Cuba, for the 1990 Simon Bolivar Award. Dr. Barrientos's lecture will be titled "Cuba: The Evolution of the Mental Health Model."

With the burgeoning Hispanic population in the United States, the committee sees a need to translate into Spanish many of the publications and press releases issued by APA, and it offered to translate this literature.

Wars raging in different parts of the world prompted the committee to consider a symposium on the impact of war on children for the 1991 annual meeting. The committee will consult relevant components to cover as many aspects of the topic as possible.

The *Committee on Occupational Psychiatry*, Peter L. Brill, M.D., chairperson, plans to develop a curriculum on occupational psychiatry and will seek funds for this project. To familiarize other psychiatrists with occupational psychiatry, the committee is establishing a network of psychiatrists working or interested in occupational psychiatry. The committee hopes to hold a day-and-a-half meeting of 20 to 25 key people in occupational psychiatry to define the field and discuss its development.

In March the committee held a meeting in Cambridge, Mass., during which it discussed its place in the component structure. At the behest of the Joint Reference Committee, Dr. Brill and the chairpersons of the Councils on Economic Affairs, National Affairs, and Psychiatric Services discussed the possible transfer of the committee. All agreed that the committee should report to the Council on Economic Affairs, and this transfer was proposed by Dr. Sata to the Joint Reference Committee in October.

Mr. Joseph Montville of the U.S. Department of State spoke to the *Committee on Psychological Aspects of Nuclear Issues*, Judith E. Lipton, M.D., chairperson. He discussed the role of behavioral understanding in international affairs and suggested that the committee bring to people's attention how enmity results from prejudice and stereotyping and why we need a period of healing and mourning. He also suggested that the committee look at destructive charismatic leaders and assess the danger they pose in the nuclear age.

Dr. Stephen Sonnenberg, a guest at the committee meeting, described a study that examined the validity of the theory of deterrence. The study found the theory flawed because of its dogmatism, its creation of a permanent "threat cycle," its failure to consider the powerful roles of affect and personality, and its failure to take into account differing world views.

The committee put together a bibliography on psychological aspects of nuclear war, copies of which are available from the APA Office of Minority/National Affairs. The committee will update the bibliography as warranted.

The members were heartened to hear that some of their efforts have borne fruit. An article in *Newsweek* (1) described the work of Dr. Vamik Volkan and others in applying psychological understanding to international conflict. The idea that international conflict involves externalization, projection, and a psychological need for enemies seems to be gaining acceptance in the popular press.

The second encouraging incident was a chance meeting between Mr. Robert Del Tredici, a Canadian photojournalist, and Dr. Igor Bocharov, who told Mr. Del Tredici that not only had Gorbachev read Dr. Judith Lipton's book *The Cave Man and the Bomb* but he was impressed by it and "it has influenced his thinking on disarmament."

The *Committee on Religion and Psychiatry*, Marc Galanter, M.D., chairperson, chose Peter Gay, Ph.D., for the 1990 Oskar Pfister Award. Dr. Gay is Sterling Professor of History at Yale University.

The Assembly reviewed a proposed position statement on religious beliefs and psychiatric treatment and suggested further revisions, which Dr. Richard Thurrell is doing. He will submit the latest revision to the Assembly in November. He has also undertaken work with 75 district branches to establish local committees on religion and psychiatry.

Drs. Marc Galanter and Paula Dobbs-Wiggins are studying the nature of psychiatric practice among organized Christian evangelical psychiatric groups. They presented their findings to the committee.

Nada L. Stotland, M.D., chairperson of the *Committee on Women*, led the discussion on reproductive choice and doctor-patient advocacy at a meeting with the Joint Commission on Government Relations. The committee feels that recent and anticipated Supreme Court and legislative decisions have seriously compromised reproductive choice, the privacy of the doctor-patient relationship, and the practice of psychiatry vis-à-vis reproductive choice. The committee urged the following courses of action: continue to lobby for reproductive choice and doctor-patient autonomy, offer and support educational activities that inform psychiatrists about the scientific evidence of psychiatric concomitants of reproductive alternatives and about the impact of new governmental decisions and pending legislation on mental health and the practice of psychiatry, identify an APA member in each district branch to participate in a national network on reproductive choice, and be an amicus curiae in relevant lawsuits.

The committee received funds for a women's activity center at the 1990 annual meeting in New York. There will be special meetings at the center: 1) "Meet the Women Leaders of APA," 2) "Board Certification and Women," 3) "Advancement in the APA Structure," 4) "How to Write a Scientific Paper," and 5) "National and Local Committees on Women."

Drs. Leah Dickstein and Sidney Fleming are refining the proposed curriculum on gender, which the committee will submit to the Committee on Graduate Education for inclusion in a compendium of transcultural curricula to be offered to residency training programs.

## REFERENCE

1. Gelman D: Why we all love to hate. Newsweek, Aug 28, 1989, pp 62–64

# The Council on Psychiatric Services

J. Frank James, M.D., Chairperson

The Council on Psychiatric Services has a strong commitment to representing the needs of patient populations and the interests of psychiatrist constituencies. It must also attempt to strengthen and update various modalities of care and treatment. From time to time urgent issues require immediate attention and feedback to the field and the APA leadership. At its meeting this past October, the council identified quality of care as the concern by which all of its component efforts should be measured. These themes will be reflected in the reports on the continuing efforts of the council and its components.

The *Task Force on Professional Practice Issues in Organized/Managed Care Settings*, Haroutun Babigian, M.D., chairperson, produced "Guidelines for Psychiatric Practice in Community Mental Health Settings" and "Guidelines for Psychiatric Practice in Staff Model Health Maintenance Organizations." These guidelines were approved by the Board of Trustees, and single copies are available at no charge from the Office of Psychiatric Services. On the recommendation of this task force, the Committee on Managed Care was established, under the auspices of the Council on Economic Affairs. In addition, this task force recommended development of a separate component to address the many issues facing psychiatrists who practice in community psychiatry settings. Although it was not possible to develop a separate new component, the council agreed that greater attention must be given to these issues. Consequently, the Committee on State Mental Health Systems will be modified to include more community psychiatrists, its charge will be revised to reflect these expanded interests, and its name will be changed to the Committee on State and Community Psychiatry Systems. Because the task force had completed its charge, it was disbanded at the end of the year with an expression of appreciation from the Board of Trustees.

Under the auspices of the Council on Psychiatric Services, a steering committee, chaired by Naomi Goldstein, M.D., and including several members of the Task Force on Professional Practice Issues in Organized/Managed Care Settings, planned and held a resource symposium in late 1988 on psychiatry and managed care. A report on the issues and possible stances for APA to consider has been developed by the steering committee and referred to the Board, the Assembly, and many APA components for discussion and debate and to the Council on Psychiatric Services for feedback. Because there are numerous issues related to managed care on which the field has not reached consensus, the council believes that it will be some time before any particular positions can be adopted. A separate informational report on the proceedings of the conference is also under development.

At the instigation of the Assembly and in conjunction with representatives of the Assembly and the Committee on Ethics, the Council on Psychiatric Services produced a brief statement titled "Guidelines Regarding Psychiatrists' Signatures." The guidelines generally address situations in which a psychiatrist might be signing a treatment plan, a prescription, or a reimbursement claim form. The statement was approved by the Board and was published in the October 1989 issue of the *American Journal of Psychiatry* (1).

The *Committee on Veterans Affairs*, Fred Guggenheim, M.D., chairperson, focused on issues important to patients in the Veterans Administration (VA) system, who represent one out of every eight psychiatric admissions in the United States. It also focused on recruitment and retention of psychiatrists working within the VA system. The committee recommended, and the Board approved, APA endorsement of a proposal to add 50 new geriatric fellowship positions within the VA; these would, of course, emphasize geriatric psychiatry. The committee also recommended that APA support the principles outlined in the report of the President's Quadrennial Commission on Pay and that APA continue to lobby for the designation of psychiatry as a scarce specialty within the VA system. These actions, which were approved by the Board, attempt to enhance pay and working conditions for VA psychiatrists. The committee also recommended that APA indicate strong support for the retention of professional (physician) administrators in the VA central office, intending to counteract a cost-saving measure that would, if effected, decrease physician participation in the decision making and medical direction of VA programs.

The *Committee on State Mental Health Systems*, Steven Katz, M.D., chairperson, encouraged involvement of the district branches in development of the states' comprehensive plans for mental health services, plans that are designed to get mental health funds through federal block grants. The committee is gratified by the large number of responses from district branches that described their efforts to influence the development of state plans. To assist in these local efforts, the committee recommended that APA ask the National Institute of Mental Health (NIMH) to be sure that meaningful input from psychiatrists is required in the central office of mental health authorities in each state and that this requirement be accomplished through the implementation of Public Law 99–660.

Noting that only three states now have psychiatrists as directors of mental health programs, the committee encouraged the National Association of State Mental Health Program Directors to facilitate regular meetings for medical directors of state (and some major city) programs so that they could identify issues and problems, exchange ideas, and develop strategies. The committee hopes to institute a newsletter for psychiatrists working in public settings within the next year.

The *Task Force on Psychiatric Services in Jails and Prisons*, Henry C. Weinstein, M.D., chairperson, completed its charge in 1989 with the production of task force report 29, which focuses on principles and guidelines for the delivery of services in jails and prisons. Single copies of the report are available at no charge from the Office of Psychiatric Services. The task force was disbanded with an expression of appreciation from the Board of Trustees. Recognizing that a large population is served in these settings and that difficulties in service delivery continue, in midyear the Board of Trustees created the Committee on Psychiatric Services in Jails and Prisons, whose activities are subject to available funding.

The *Committee on Psychiatric Services in the Military*, Leonora Petty, M.D., chairperson, highlighted current conflicts concerning qualifications and scope of practice in its report on the plan of the U.S. Department of Defense to initiate a pilot program whereby nonphysician mental health professionals would be taught to prescribe medications. APA had strenuously argued the inappropriateness of this program and continues to do so. On recommendation of the committee and the council, the Board of Trustees reaffirmed its commitment to ensuring that medical differential diagnosis and treatment planning are required for patients and patient populations with mental health problems and that hospital admitting privileges and prescription-writing privileges are granted only to those who have appropriate medical education, orientation, training, and experience. The committee also reported an anticipated reduction in the available mental health budget and program for CHAMPUS beneficiaries. It urged APA to encourage careful review of the factors and statistics that led to this decision by the Department of Defense and encouraged APA to use its offices to influence decisions and to call on the American Medical Association to assist with lobbying efforts.

The *Committee on the Chronically Mentally Ill*, Stephen Goldfinger, M.D., chairperson, continues to provide educational opportunities at APA's annual meeting and elsewhere. Currently, it is working with the APA Survey Design and Analysis Department to analyze data obtained in the recent biographical survey concerning chronically ill populations treated by psychiatrists. After 2 years of working with other organizations, the committee achieved publication in the *American Journal of Psychiatry* of its basic residency curriculum for treatment of the chronically mentally ill (2). The committee remains hopeful that APA will be able to endorse the report and its recommendations.

The *Committee on Rehabilitation*, Arthur Meyerson, M.D., chairperson, has undertaken development of a definition of psychiatric rehabilitation, which will address acuteness and severity of illness as they bear on the need for psychiatric rehabilitation and funding patterns that appropriately distinguish, yet support, treatments for psychiatric illness directed at both acute care and rehabilitation. The committee continues to be APA's liaison to the Rehabilitation Services Administration and the President's Committee on Employment of the Handicapped. Dr. Arthur Meyerson represents APA on advisory committees to both of these agencies.

The *Task Force on the Homeless Mentally Ill*, Frederic Kass, M.D., chairperson, held its first meeting in September. It includes one member, the chairperson, and designated representatives from about 10 relevant APA components. The task force will produce a report on what has and has not changed since the 1984 publication of APA's *The Homeless Mentally Ill*. It has submitted a proposal for a workshop on the mentally ill homeless at the 1990 annual meeting. Designated representatives were asked to think of efforts they might promote on behalf of the homeless mentally ill in their respective committees and councils.

The *Task Force on Psychiatric Services for Mentally Retarded/Developmentally Disabled Adults*, Ludwik Szymanski, M.D., chairperson, is addressing psychiatrists' lack of participation in the field of mental retardation. To develop its report, the task force will rely on a literature review, but its members also conducted a questionnaire survey of all child and adult psychiatry training programs in the country and all state departments of mental health and mental retardation. It also requested comments from major professional organizations that have an interest in this field. The task force perceives several trends and is hoping to have a draft report by May 1990.

The *Task Force on Clinician Safety*, William Dubin, M.D., chairperson, has reviewed the literature and has conducted a survey of about 300 residents in Pennsylvania. Psychiatrists and institutions tend to deny the risk of violence, so the task force has also focused on consciousness raising. At the 1989 meeting, the task force sponsored a symposium and a workshop, which were well attended. Psychiatrists who had been assaulted were asked to identify themselves, and approximately 50 did. A member of the task force followed up with phone interviews. The committee has also established liaisons with representatives of a number of other APA components, and it has met with security experts. The task force can foresee several possible products, including an informational report, guidelines, and recommendations.

The *Committee on Liaisons with the American Hospital Association*, Stuart Keill, M.D., chairperson, continues to meet with its counterpart at the American Hospital Association. The joint committee of the two associations reviews recently enacted and upcoming government legislative and regulatory activities to alert their parent organizations of shared interests and concerns. The committee has also written to the Joint Commission on the Accreditation of Healthcare Organizations (JCAHO) to obtain clarification of the survey of managed care settings and the criteria by which psychiatric services will be surveyed.

The Institute on Hospital and Community Psychiatry Program Committee, Leonard Stein, M.D., chairperson, planned and held the successful 1989 Institute, which included a number of special presentations on dual diagnosis and psychiatric services for the hearing impaired. The attendance at the Institute continues to increase each year. The program offerings have become rich and complex, while the atmosphere of a smaller-scale meeting has been maintained. Plans for next year's Institute in Denver are under way, under the leadership of James Barter, M.D., the committee's new chairperson.

The *Committee to Coordinate the H&CP Service, Journal, and Institute*, H. Richard Lamb, M.D., chairperson, reported that the service has transferred substantial funds to the *H&CP* journal to support Service members' subscriptions to the journal. The total number of journal copies distributed through the Service as of midyear 1989 was approximately 10,000. The Psychiatric Placement Service was organized to help hospitals find qualified psychiatrists for vacant positions. Although this service is available to all facilities, Service members are charged a lower fee. The Service has been asked a number of times to conduct executive searches. It was not designed to perform this in-depth function, but a pilot program of a small number of executive searches will be attempted in the coming year. The experience gained will be evaluated to see if the executive search function will continue. In addition to the journal and the placement service, a number of other benefits are offered through the H&CP Service, including access to a video library. The Service issued a new video library catalog late in 1988.

The *Committee on the Practice of Psychotherapy*, Marcia Kraft Goin, M.D., chairperson, has continued to develop a generic document, "The Role of Psychotherapy in Psychiatric Practice." The committee will use this document as a basis for spinoffs edited for targeted audiences, such as nonpsychiatric physicians, consumers, insurance executives, and legislators. In the last several years the committee has presented educational programs during the APA annual meeting that focus on psychotherapy in the treatment of specific disorders. One focused on the role of psychotherapy in the treatment of depression and the other on the role of psychotherapy in the treatment of schizophrenia. These presentations were videotaped and are available from the APA library to APA members. In 1990 the committee hopes to present a program on the role of psychotherapy in the treatment of disease involving the human immunodeficiency virus (HIV); it is hoped that this program also can be videotaped and made available to members. The committee has established liaison with the chairperson of APA's Work Group on the Harvard Resource-Based Relative Value Scale Study to gain understanding and provide input on the aspects of care, particularly concerning psychotherapy, that will be addressed.

The *Committee on Private Practice*, Boris Rifkin, M.D., chairperson, again sponsored several educational and informative activities during APA's annual meeting. A day of workshops on private practice issues was presented and covered such topics as setting up a private practice, professional liability, legal issues, coding and current procedural terminology, the resource-based relative value scale, managed care, and third-party payers. The committee will hold similar workshops in 1990. In addition, it will sponsor an invitational forum for private practitioners, which will offer a brief program and an opportunity for exchange of information. Because the size of the invitational forum must be limited, it was agreed that several representatives from each district branch will be invited.

This year a major concern of the council, as well as of the public, was alcohol and drug abuse. Addictive disorders are found in people of both sexes, all ages, and all ethnic groups and sections of society and have caused particularly severe suffering among minority communities. Individuals with these disorders are seen in private offices, hospitals, mental health facilities in both public and private systems, jails, and work-related outpatient programs. The *Committee on Drug Abuse*, Edward Kaufman, M.D., chairperson, and the *Committee on Alcoholism*, Richard Frances, M.D., chairperson, jointly recommended the establishment of the Council on Addiction Psychiatry within APA. This new council will foster and provide leadership in prevention, education, treatment, research, and policy development for American psychiatry in the addiction field. It will represent a body of knowledge, skills, and experience indispensable to the advancement of quality care for substance-abusing patients. The council will assure that general psychiatric trainees and practicing psychiatrists are supported in providing care for addicted patients that meets the highest standards. It will provide a strong voice in the formulation of policy, will increase interest in and visibility of addiction disorders within psychiatry, and will provide liaison to the many government and voluntary organizations active in this field. The Board of Trustees gave its approval to establishment of the new council, subject to available funding and staffing to support it.

The Committee on Drug Abuse is presently working on several documents. One will address drugs of abuse in schools and will replace the 1969 APA position statement on the same topic, which was rescinded late last year. The other will address prevention, assessment, diagnosis, and treatment of psychoactive substance abuse. Both the Committee on Alcoholism and the Committee on Drug Abuse continue to discuss the possibility of added qualifications in addiction psychiatry. This recommendation, however, has not yet been reviewed by the overall APA components addressing new subspecialty areas. Both committees favor subspecialties within major specialties rather than the formation of separate groups outside the major specialty groups. These committees continue their liaison with the National Institute on Drug Abuse and the National Institute on Alcoholism and Alcohol Abuse.

The council itself considered a number of important items during the year. It heard a report from Ira Glick, M.D., science advisor to the director of NIMH, about national initiatives on behalf of the severely mentally ill. These include the development of a national plan of research to improve care for patients with severe mental disorders. Although that project is well under way at NIMH, the council has established a liaison to provide feedback on various topics. The council noted the movement within the JCAHO to return state hospitals to survey under the *Consolidated Standards*, rather than the *Accreditation Manual for Hospitals*. APA has consistently supported the latter for all psychiatric hospitals. The council supported the formation of a JCAHO task force to resolve the issue and encouraged APA to take an active role in helping all parties, including the state hospital facilities, to deal with their specific problems.

The council prioritized a number of areas in which APA might promote data collection and analysis. Input by the council and other components will be reviewed by the APA Work Group on National Data Bases for Psychiatry. Data development would enhance APA's arguments in certain areas. Roughly in order of importance to the council, these areas are access to services, economics of practice, patterns of practice, professional development, quality of care, the public-sector patient, organization of services, external reviews, dissemination of knowledge, public perception of psychiatry, interprofessional relations, patients with multiple disabilities, monitoring physician competence, special populations, and confidentiality.

The council considered several Assembly action papers during the year. One supported the formation of a component on family systems and family therapy and was explored with representatives of the Family Systems Caucus. Subsequently, the council recommended establishment of a task force, which was approved and will begin its work sometime in 1990. A second Assembly action paper that was considered addressed members' questions about the payment of Medicare claims. One result of that action paper was the establishment of an 800 telephone number that members can call for assistance from an APA staff Medicare specialist. The action paper also suggested a national component on Medicare, but the council felt that consultation on specific Medicare problems could probably be best handled through regional or local contacts with psychiatrists.

The council asked its Committee on Private Practice to discuss this matter further, and it also suggested that the Assembly consider identifying local psychiatrists who could be contacted through the district branches.

The council reviewed a statement of goals developed by the Long Range Planning Committee. In general, the council thought the document gave limited attention to service delivery issues and suggested that additional emphasis be placed on such matters in the future.

It has been a busy and rewarding year. The council anticipates several challenges in the coming year, including matters relating to homeless mentally ill persons, care of the indigent, and quality of care. Some realignment of the council structure may be necessary for greater efficiency.

## REFERENCES

1. Guidelines regarding psychiatrists' signatures. Am J Psychiatry 1989; 146:1390
2. Faulkner LR, Cutler DL, Krohn DD, et al: A basic residency curriculum concerning the chronically mentally ill. Am J Psychiatry 1989; 146:1323–1327

# The Council on Psychiatry and Law

Howard Zonana, M.D., Chairperson

The council has been busy this year coming to closure on and initiating projects related to laws that regulate psychiatric practices and to the use of psychiatric expertise in the resolution of legal issues.

As was reported to the APA membership in the *Journal* a year ago, the council's proposed model regulation concerning the patient's right to refuse medication was reviewed by a representative group from the Assembly. The council reviewed a series of state court decisions that were establishing judicial review of treatment refusal for cases reaching appellate review. Given this trend, the council felt it was important that states which do not yet have mandated judicial review have some viable alternatives to recommend to state legislatures. For that reason, the council, which initially had proposed the model regulation be formally adopted as APA policy, requested that it be approved as a resource document so it could be circulated quickly. The Assembly, however, had developed its own proposed document, which differed from the council's and from APA's position in various amicus briefs on this subject. The Assembly recommended that both documents be circulated as resource documents. The Joint Reference Committee felt that circulating two documents on the same topic with contrasting views would not be helpful to the district branches. In an effort to resolve the issue, the Joint Reference Committee appointed a working group on the right to refuse medication to try to resolve the differences in the two documents and produce one document. The working group was chaired by President-Elect Benedek and had representative membership from the Assembly, the council, and the Commission on Judicial Action. The working group met and produced a document on which all members agreed. This document was presented to the Joint Reference Committee in October and to the Assembly in November. The council hopes that the document will be approved as a resource document by the Board in December. It was also agreed that the council would review the situations in the states which had mandated judicial review for refusals of medication in order to understand the problems and any possible benefits.

The council continued to examine the issue of reporting mentally ill persons to departments of motor vehicles. As a first step, the council reviewed various state laws on this subject and will contact related medical specialty societies that have similar concerns in this area. This discussion was precipitated by a review of several cases, such as *Naidu v. Laird* (1), *Cain v. Rijken* (2), and *Schuster v. Altenberg* (3), in which liability was imposed on mental health professionals when patients or former patients were released from the hospital and later involved in automobile accidents that resulted in the deaths of third parties.

During the fall component meetings, the council responded to a request from APA's Commission on AIDS to review a proposed position statement on mandatory reporting of persons testing positive for the human immunodeficiency virus. The council members opposed mandatory reporting, feeling that such action would not assist in public health efforts and would merely be an unnecessary intrusion into patients' privacy.

A November 1988 Area V action paper titled "Physician-Assisted Euthanasia" was referred to the council by the Joint Reference Committee. The council recommended to the Joint Reference Committee that an ad hoc committee with representatives from the council, the Council on Aging, and the Ethics Committee be established so that a thorough examination of the ethical, moral, and legal implications of this issue can be made. Psychiatrists frequently become involved in assessments of competency when patients refuse treatment and when decisions limiting treatment are made.

The council reviewed several guidelines from the Council of Medical Specialty Societies and the American Medical Association regarding physicians who act as expert witnesses. There have been many prior council discussions regarding the difficulties of reviewing testimony and depositions by APA members. There was renewed interest in submitting a few transcripts and attempting to see what types of reviews are possible.

Dr. Zonana has been working extensively with staff from the office of U.S. Representative Barbara Boxer (D-Calif.), who is drafting legislation regarding civil commitment and the military. Representative Boxer's office has received complaints and conducted hearings regarding the inappropriate hospitalization of military whistle-blowers in psychiatric hospitals. Dr. Zonana has been working to bring the draft legislation into agreement with APA's "Guidelines on Legislation on the Psychiatric Hospitalization of Adults."

Additional issues that the council is addressing include development of guidelines for expert testimony and initial discussions of the implications for psychiatry of the recent Supreme Court decision in the *Webster* case, which involved abortion.

The *Committee on Confidentiality*, Aron Wolf, M.D., chairperson, has continued to address confidentiality concerns brought to its attention by APA members. Additionally, the committee was asked by the council to develop guidelines regarding confidentiality in evaluations on behalf of third parties, such as a court, employer, government agency, prison, and Workmen's Compensation. The committee held a workshop on this topic during the 1989 annual meeting. The vignette format used for this workshop and the feedback from the audience has given the committee a focus with which to begin developing the written guidelines.

The committee, at the instruction of the Joint Reference Committee, will serve as coordinator of responses by various APA components to the Area III Assembly action paper "The Role of the Psychiatrist When Requested to Provide Information About Patients for Security Clearances." The U.S. Defense Investigation Service now routinely asks psychiatrists who have treated patients applying for security clearances to provide information about these patients.

The *Task Force on Disclosure of Psychiatric Treatment Records in Child Custody Disputes*, Carl Malmquist, M.D., chairperson, continues to develop a task force report on issues involving access to a parent's psychiatric records in child custody disputes.

The *Task Force on Use and Misuse of Psychiatric Diagnoses in the Courts*, Seymour Halleck, M.D., chairperson, hopes to have a final draft of its task force report by May 1990. The document describes the appropriate use of psychiatric diagnosis and is intended to assist the courts in evaluating capacities without over- or understating the importance of the specific diagnosis. It also is attempting to deal with the difficult issues of the legal concept of disease and its implications for responsibility for behavior.

## REFERENCES

1. Naidu v Laird, 539 A 2d 1064 (Del 1988)
2. Cain v Rijken, 717 P 2d 140 (Ore 1986)
3. Schuster v Altenberg, 424 NW 2d 159 (Wis 1988)

# The Council on Research

Jack Barchas, M.D., Chairperson

Through its work and that of its components, the Council on Research seeks to influence science policy, undertake scientific assessment and evaluation, support and broaden psychiatric research and research training opportunities, and provide policy guidance for APA research activities.

To that end, the council regularly communicates with federal research agencies, and 1989 was no exception. This year, the council met with key leaders of the agencies of the Alcohol, Drug Abuse, and Mental Health Administration (ADAMHA), including the administrator of ADAMHA and the directors of the National Institute of Mental Health (NIMH), the National Institute on Alcohol Abuse and Alcoholism, and the National Institute on Drug Abuse. These meetings addressed research training, animal research, medical and lay educational needs, scientific misconduct, and conflicts of interest and continued the ongoing discussion of APA's advocacy of ADAMHA research appropriations.

A number of policy issues figured prominently in council deliberations, among them animal research, research priorities for child and adolescent mental disorders, and conflicts of interest in scientific research. In regard to animal research, the council again stressed the importance of this issue and the need for APA to take a leadership role by adopting a policy statement on the appropriate and necessary use of animals in research. The document drafted by the council was subsequently endorsed by the Board of Trustees. A cover letter from APA President Herbert Pardes, M.D., and a fact sheet on animal research issues developed by the APA Division of Public Affairs will be distributed to all members of APA. The council received the report of the Institute of Medicine on research priorities for child and adolescent mental disorders, which spoke clearly of the overwhelming need for additional support for such research. With that goal in mind, the council plans to establish a small working group to work with the Council on Children, Adolescents, and Their Families in an effort to ensure that the Institute of Medicine's funding and research recommendations are implemented. Finally, the council, in collaboration with the Joint Commission on Government Relations, developed comments on scientific misconduct regulations proposed by the Department of Health and Human Services.

The council continues to administer the Lilly Psychiatric Research Fellowship and the Kempf Fund Award for Research Developments in Psychobiological Psychiatry. The former award is a 1-year fellowship given to a postgraduate medical trainee for research and personal scholarship. The Kempf award recognizes a senior researcher who has made a significant contribution to research on the causes and treatment of schizophrenia and also provides partial support for the career development of a young research psychiatrist working in a trainee-mentor relationship with the senior winner. The winners of the 1989 Kempf award were Charles Nemeroff, M.D. (senior awardee) and Lawrence A. Dunn, M.D. (junior awardee), and James H. Meador-Woodruff, M.D., received the Lilly Psychiatric Research Fellowship.

As in the past 2 years, in 1989 the council joined the Office of Research in hosting a by-invitation-only breakfast for young researchers at APA's annual meeting; more than 125 attended. The attendees not only had an opportunity for informal exchange with colleagues and senior researchers but were treated to an informative presentation by NIMH Director Lewis Judd, M.D. Moreover, in an exciting new collaborative undertaking with the Scientific Program Committee and the Office of Research at the San Francisco meeting, the council inaugurated the Young Investigators Poster Session, which was limited in size only by the available space. Some 80 researchers in the early stages of their careers had the opportunity to discuss their works in progress with both their colleagues and a large number of senior investigators who attended the session. The council anticipates that this new annual meeting event will continue to grow and generate excitement.

Finally, the council sadly reports the untimely death of John E. Adams, M.D., chairperson of the department of psychiatry at the University of Florida and past chairperson of the Council on Research. Dr. Adams's influence will be greatly missed by the Office of Research, by this council, and by psychiatry.

Following are details of the activities of components under the Council on Research.

Since last year, the report of the *Task Force on Treatments of Psychiatric Disorders*, T. Byram Karasu, M.D., chairperson, was published and the task force disbanded with the council's appreciation for its dedicated work. The council was extremely pleased both with the favorable reviews the report received and with its excellent sales.

The new *Task Force on Neuropsychiatric Aspects of Traumatic Brain Injury* was approved by the Board of Trustees in late 1989 and now awaits funding and appointment of members.

The *Committee on Research on Psychiatric Treatments*, John Kane, M.D., chairperson, oversees APA treatment assessment activities and responds to scientific issues regarding psychiatric treatment. It has developed a protocol through which topics for consideration are selected and assessed by either the committee itself or an established or new task force. Most recently, after the discharge of the Task Force on Treatments of Psychiatric Disorders, the committee was charged with the development of guidelines for the updating and publishing of future editions of *Treatments of Psychiatric Disorders.*

In addition, the committee is concerned with the broad range of science policy issues affecting research on psychiatric treatments. Recent changes in U.S. Food and Drug Administration policy on reviewing experimental drugs, reimbursement for the clinical costs of research, pharmaceutical industry investment in development of psychiatric drugs, and malpractice coverage for use of nonapproved drugs are some of the issues considered by the committee. For example, at the 1989 fall meetings the committee sought to broaden dialogue with NIMH. The committee met with NIMH Senior Science Advisor Ira Glick, M.D., for a wide-ranging discussion of the representation of psychopharmacologic and psychosocial treatment research on the NIMH agenda.

The subcommittee to review anticonvulsants in psychiatry has undertaken a comprehensive review of nearly 500 articles on the subject. A small committee work group will undertake a preliminary investigation of issues involving nicotine dependence.

Further, the Committee on Research on Psychiatric Treatments oversees a variety of treatment-related task forces, including the Task Force on Electroconvulsive Therapy, the Task Force on Tardive Dyskinesia, the Task Force on Benzodiazepine Dependency, the Task Force on Psychosocial Treatment Research, and the Task Force to Study the Long-Term Effects of Lithium on the Kidney. Summaries of their activities follow.

The *Task Force on Benzodiazepine Dependency*, Carl Salzman, M.D., chairperson, completed its work of 2 years and presented its final report to the Council on Research in May 1989. The report covers toxicity, dependence, and abuse of benzodiazepines and, consistent with the task force's charge, does not contain recommendations for prescription or clinical use. The task force was assisted by a number of national and international experts in psychopharmacology and benzodiazepines. More than 1,500 references were reviewed to prepare the report.

The council commended the task force for the comprehensiveness and high quality of its assessment of the extensive scientific information in this complex and controversial area. A condensed version of the task force document is being prepared for submission to the *American Journal of Psychiatry*; the entire report will be published as part of the APA task force report series.

Responding to its charge, the *Task Force on Electroconvulsive Therapy*, Richard Weiner, M.D., chairperson, submitted its final report, "The Practice of ECT: Recommendations for Treatment, Training and Privileging," to the Committee on Research on Psychiatric Treatments and to the Council on Research in September 1989. The document contains a series of recommendations regarding treatment, training, and privileging in ECT. It also includes a rationale for these recommendations and a detailed bibliography of ECT-related literature. If approved by the Board of Trustees, the report will be published by the American Psychiatric Press, Inc., as an APA task force report. Both the task force and the Council on Research hope for wide distribution of the report's recommendations through presentations and publication reprints. The task force plans to present a workshop at the 1990 APA annual meeting, to devote a segment of the annual meeting's ECT course to the report's recommendations, and to develop presentations for a number of scientific meetings.

The *Task Force on Psychosocial Treatment Research*, John Docherty, M.D., chairperson, expects to complete its report within the next few months. In the report the task force will identify the current state of the art in psychosocial treatment research, describe problems confronted by the field, present questions, new developments, and treatment implications of psychosocial treatment research, and make recommendations for future science and public policy.

The *Task Force to Study the Long-Term Effects of Lithium on the Kidney*, George Heninger, M.D., chairperson, continues its work.

The *Task Force on Tardive Dyskinesia*, John Kane, M.D., chairperson, has nearly completed its report, which will be geared toward the clinician rather than the researcher. The multichapter book will include a chapter on forensic issues and may include all existing rating scales for tardive dyskinesia. The Committee on Research on Psychiatric Treatments hopes approval and publication will occur in early 1990.

The *Committee on the Biographical Directory and Research on Psychiatric Professional Activities* (formerly the Committee on the Biographical Directory and Related Research), Robert Dorwart, M.D., chairperson, reported publication of the *Biographical Directory* in early 1989. Collection of the survey data on nonmembers has been completed. The committee now is reviewing the process by which that publication was produced and may suggest modifications to that process for the next directory. The committee is also preparing an overview article detailing the characteristics and professional activities of U.S. psychiatrists as the first step in its analysis of the data collected from the professional activities survey.

Dr. Dorwart also serves as chairperson of the newly established APA Work Group on National Data Bases for Psychiatry, which will identify data collection and analysis projects APA should undertake to ensure independent research on policy issues. That work group has begun to identify policy issues and to determine data needs based on those issues.

The *Committee on Research Training*, Ronald Rieder, M.D., chairperson, was established in 1989 to highlight the importance of increasing the number of psychiatric researchers, to improve the quality of research training, and to expand the range of opportunities for psychiatrists who wish to enter training careers. The committee was charged with the examination of issues relating to funding, the training environment, retention of researchers, and the roles of research mentors. The committee will work with the Office of Research to try to influence NIMH to expand support of medical student training and to increase the number of postresidency research training fellowships in psychiatry. It will serve as a focal point in coordinating APA activities related to research training. The committee will also examine related policy issues at both the national and local levels.

The Committee on Research Training held its first organizational meeting in fall 1989, at which time it agreed to plan a national conference on psychiatric research training to gather data and evaluate the state of the art, help remove some of the impediments to research careers, develop a mechanism for matching trainees and directors, and formulate an agenda for the future. Committee members also proposed a component workshop on research training for the 1990 annual meeting and the development of a young investigator award.

The *Task Force on Prevention Research*, Robert Rose, M.D., chairperson, is developing a brief report that contains a summary of where the field currently stands, recommendations for future prevention research, and suggestions on how APA might facilitate these recommendations.

The *Committee on Psychiatric Diagnosis and Assessment*, Layton McCurdy, M.D., chairperson, continues to monitor and give advice on the development of *DSM-IV*. The committee supervises work on *DSM-IV* and will develop suggestions and recommendations for how the manual can best be interpreted and considered in nonclinical settings. Representatives of the committee will work with the Task Force on Use and Misuse of Psychiatric Diagnoses in the Courts in this effort.

The committee is also responsible for handling and reviewing all issues involving scientific assessment of diagnostic issues. In this capacity it will also supervise the work of the Task Force on Quantitative Electrophysiological Assessment.

The development of *DSM-IV* by the *Task Force on DSM-IV*, Allen Frances, M.D., chairperson, has been divided into three stages. The first, literature reviews for all diagnostic categories (conducted by individual work groups), are under way; many already have been completed. The second stage, reanalysis of existing data sets, will be supported by a grant from the John D. and Catherine T. MacArthur Foundation. In this process, work group members may apply for support of multisite analysis of existing data sets to answer questions that are not resolved in the literature review. Approximately 30 applications for funding of these activities have already been received. Should outside funding be obtained, the third stage will consist of field trials to answer questions that remain unresolved after stages one and two. Field trials will also be used to assess the overall reliability of the *DSM-IV* system. Progress in the development of *DSM-IV* is regularly summarized for interested individuals and organizations in the Office of Research's semiannual newsletter, *DSM-IV Update*. Members interested in receiving the newsletter should contact the APA Office of Research.